EXHIBIT J - PART 2 OF 2

PTO/SB/22 (06-09)
Approved for use through 06/30/2009. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARMENT OF COMMERCE

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a) **FY 2009** (*Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).*)	Docket Number (Optional) CELG-0508
Application Number 11/437,551	Filed 2006-05-19
For Methods For Delivering A Drug to A Patient While Restricting Access To The Drug By Patients For Whom	
Art Unit 3769	Examiner Sharick Naqi

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

		Fee	Small Entity Fee	
☐	One month (37 CFR 1.17(a)(1))	$130	$65	$
☐	Two months (37 CFR 1.17(a)(2))	$490	$245	$
☑	Three months (37 CFR 1.17(a)(3))	$1110	$555	$ 1110.00
☐	Four months (37 CFR 1.17(a)(4))	$1730	$865	$
☐	Five months (37 CFR 1.17(a)(5))	$2350	$1175	$

☐ Applicant claims small entity status. See 37 CFR 1.27.

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☑ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 233050.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest. See 37 CFR 3.71.
Statement under 37 CFR 3.73(b) is enclosed (Form PTO/SB/96).

☑ attorney or agent of record. Registration Number 51430

☐ attorney or agent under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

/Stephanie A. Barbosa/ — Signature

June 29, 2009 — Date

Stephanie A. Barbosa — Typed or printed name

(215) 568-3100 — Telephone Number

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below.

☑ Total of 1 forms are submitted.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

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3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
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5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

DOCKET NO.: CELG-0508 **PATENT**
Application No.: 11/437,551
Office Action Dated: January 8, 2009

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Bruce A. Williams and Joseph K. Kaminski

Confirmation No.: **3533**

Application No.: **11/437,551**

Group Art Unit: **3769**

Filing Date: **May 19, 2006**

Examiner: **Sharick Naqi**

For: **Methods For Delivering A Drug To A Patient While Restricting Access To The Drug By Patients For Whom The Drug May Be Contraindicated**

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

REPLY PURSUANT TO 37 CFR § 1.116

In response to the Official Action dated **January 8, 2009**, reconsideration is respectfully requested in view of the amendments and/or remarks as indicated below:

☐ **Amendments to the Specification** begin on page of this paper.

☒ **Amendments to the Claims** are reflected in the listing of the claims which begins on page 2 of this paper.

☐ **Amendments to the Drawings** begin on page of this paper and include an attached replacement sheet.

☒ **Remarks** begin on page 10 of this paper.

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claims 1-31 (Canceled).

32. (Currently Amended) A method of treating a male patient, suffering from erythema nodosum leprosum, with thalidomide, ~~said method comprising~~ permitting prescriptions for thalidomide to be filled by a pharmacy only after the pharmacy has retrieved an approval code for the prescription, wherein the generation of the prescription approval code comprises the following steps:

(a) via a computer, registering a prescriber and the pharmacy with a distributor of thalidomide;

(b) determining whether the patient is able to understand and reliably carry out instructions;

(c) upon determination that the patient is able to carry out the instructions, providing oral and written warnings of the hazard of taking thalidomide and exposing fetus to the drug;

(d) further providing oral and written warnings of the risk of possible contraception failure and of the need to use barrier contraception when having sexual intercourse with women of child bearing potential;

(e) obtaining acknowledgement of said warnings from the patient;

(f) registering the patient with the distributor; and

(g) upon obtaining the acknowledgement and registration, generating via a computer the prescription approval code to be retrieved by the pharmacy before the prescription is filled; and

~~(h)~~ upon retrieving a prescription approval code, administering thalidomide to the patient.

33. (Previously Presented) The method of claim 32, wherein the acknowledgement requires the patient's acknowledgement of one or more of the following:

(a) the understanding that thalidomide must not be taken if unprotected sex cannot be avoided;

(b) the understanding of potential birth defects;

(c) that the patient has been advised of the need for barrier contraception by the prescriber;

(d) the obligation to inform the prescriber if the patient's sexual partner is suspected of becoming or being pregnant;

(e) that thalidomide is solely for the use of the patient himself and must not be shared with any other person;

(f) that the patient has read the information brochure or viewed the information film on thalidomide;

(g) that the semen or blood must not be donated during the thalidomide treatment;

(h) that all of the patient's inquiries regarding thalidomide treatment have been answered by the prescribing physician; or

(i) the patient's understanding that participation in a survey and patient registry is required during the thalidomide treatment.

34. (Previously Presented) The method of claim 32 further comprising providing the patient, prior to generation of the approval code, with warnings of the side effects associated with administration of thalidomide, wherein said side effects are non-teratogenic side effects.

35. (Previously Presented) The method of claim 32 further comprising obtaining a written authorization by the prescriber prior to generation of the approval code.

36. (Previously Presented) The method of claim 32, wherein the prescription approval code is retrieved from a computer readable storage medium.

37. (Previously Presented) The method of claim 32, wherein the acknowledgement is a written informed consent.

38. (Previously Presented) The method of claim 37, wherein the written informed consent is registered in the medium prior to generation of the prescription approval code.

39. (Currently Amended) A method of treating a female patient, suffering from erythema nodosum leprosum, with thalidomide, ~~said method comprising~~ permitting prescriptions for thalidomide to be filled by a pharmacy only after the pharmacy has retrieved an approval code for the prescription, wherein the generation of the prescription approval code comprises the following steps:

(a) via a computer, registering a prescriber and the pharmacy with a distributor of thalidomide;

(b) determining whether the patient is able to understand and reliably carry out instructions;

(c) upon determination that the patient is able to carry out the instructions, determining whether the patient is of child bearing potential;

(d) upon determining that the patient is of child bearing potential, providing oral and written warnings of the hazard of taking thalidomide and exposing fetus to the drug;

(e) further providing oral and written warnings of the risk of possible contraception failure and of the need to simultaneous use of two reliable forms of contraception;

(f) obtaining acknowledge of said warnings from the patient;

(g) determining, prior to the scheduled beginning of the thalidomide therapy, whether the patient is pregnant;

(h) registering the patient with the distributor; and

(i) generating via a computer the prescription approval code to be retrieved by the pharmacy before the prescription is filled; and

~~(j)~~ upon retrieving the prescription approval code, administering thalidomide to the patient.

40. (Previously Presented) The method of claim 39, wherein the acknowledgement requires the patient's acknowledgement of one or more of the following:

(a) the understanding that thalidomide must not be taken if the patient is pregnant, breastfeeding a baby, or able to get pregnant and not using birth controls;

(b) the understanding of potential birth defects;

(c) the warning received by the prescriber regarding said birth defects;

(d) the understanding of the need for at least two forms of contraception prior to, during, and subsequent to thalidomide treatment;

(e) the obligation to undergo a pregnancy test prior to starting thalidomide treatment;

(f) the obligation to undergo a pregnancy test during the thalidomide treatment;

(g) the obligation to discontinue thalidomide treatment and inform theprescriber in the case that the patient is suspected of becoming or being pregnant;

(h) that the patient is not currently pregnant and will not try to become pregnant for at least 4 weeks after the completion of thalidomide treatment;

(i) that thalidomide is solely for the use of the patient herself and must not be shared with any other person;

(j) that the patient has read the information brochure or viewed the information film on thalidomide;

(k) that the blood must not be donated during the thalidomide treatment;

(l) that all of the patient's inquiries regarding thalidomide treatment have been answered by the prescriber; or

(m) the patient's understanding that participation in a survey and patient registry is required during the thalidomide treatment.

41. (Previously Presented) The method of claim 39 further comprising providing the patient, prior to generation of the approval code, with warnings of the side effects associated with administration of thalidomide, wherein said side effects are non-teratogenic side effects.

42. (Previously Presented) The method of claim 39 further comprising obtaining a written authorization by the prescriber prior to generation of the approval code.

43. (Previously Presented) The method of claim 39, wherein the prescription approval code is retrieved from a computer readable storage medium.

44. (Previously Presented) The method of claim 39, wherein the acknowledgement is a written informed consent.

45. (Previously Presented) The method of claim 44, wherein the informed written consent is registered in the medium prior to generation of the prescription approval code.

46. (Currently Amended) A method of treating a male patient, suffering from erythema nodosum leprosum, with thalidomide, said method comprising permitting prescriptions for thalidomide to be filled by a pharmacy only after the pharmacy has retrieved an approval code for the prescription from a computer readable storage medium, wherein the generation of the prescription approval code comprises the following steps:

(A) registering a prescriber and the pharmacy via a computer in the computer readable storage medium;

(B) determining whether the patient is able to understand and reliably carry out instructions;

(C) upon determination that the patient is able to carry out instructions, providing oral and written warnings of the hazard of taking thalidomide and exposing fetus to the drug;

(D) further providing oral and written warnings of the risk of possible contraception failure and of the need to use barrier contraception when having sexual intercourse with women of child bearing potential;

(E) obtaining informed consent from the patient;

(F) registering the patient via a computer in the computer readable storage medium; and

(G) upon obtaining the informed consent and registration, generating the prescription approval code to be retrieved by the pharmacy before the prescription is filled, wherein said informed consent requires the patient's acknowledgement of one or more of the following:

(a) the understanding that thalidomide must not be taken if unprotected sex cannot be avoided;

(b) the understanding of potential birth defects;

(c) that the patient has been advised of the need for barrier contraception by the prescriber;

(d) the obligation to inform the prescriber if the patient's sexual partner is suspected of becoming or being pregnant;

(e) that thalidomide is solely for the use of the patient himself and must not be shared with any other person;

(f) that the patient has read the information brochure or viewed the information film on thalidomide;

(g) that the semen or blood must not be donated during the thalidomide treatment;

(h) that all of the patient's inquiries regarding thalidomide treatment have been answered by the prescribing physician; or

(i) the patient's understanding that participation in a survey and patient registry is required during the thalidomide treatment; and

~~(H)~~ upon retrieving the prescription approval code, administering thalidomide to the patient.

47. (Previously Presented) The method of claim 46 further comprising providing the patient, prior to generation of the approval code, with warnings of the side effects associated with administration of thalidomide, wherein said side effects are non-teratogenic side effects.

48. (Previously Presented) The method of claim 46 further comprising obtaining a written authorization by the prescriber prior to generation of the approval code.

49. (Currently Amended) A method of treating a female patient, suffering from erythema nodosum leprosum, with thalidomide, said method comprising permitting prescriptions for thalidomide to be filled by a pharmacy only after the pharmacy has retrieved an approval code for the prescription from a computer readable storage medium, wherein the generation of the prescription approval code comprises the following steps:

(A) registering a prescriber and the pharmacy via a computer in the computer readable storage medium;

(B) determining whether the patient is able to understand and reliably carry out instructions;

(C) upon determination that the patient is able to carry out instructions, determining whether the patient is of child bearing potential;

(D) upon determining that the patient is of child bearing potential, providing oral and written warnings of the hazard of taking thalidomide and exposing fetus to the drug;

(E) further providing oral and written warnings of the risk of possible contraception failure and of the need to simultaneous use of two reliable forms of contraception;

(F) obtaining informed consent from the patient;

(G) determining, prior to the scheduled beginning of the thalidomide therapy, whether the patient is pregnant;

(H) registering the patient via a computer in the computer readable storage medium; and

(I) generating the prescription approval code to be retrieved by the pharmacy before the prescription is filled; and

~~(J)~~ upon retrieving the prescription approval code, administering thalidomide to the patient,

wherein said informed consent requires the patient's acknowledgement of one or more of the following:

(a) the understanding that thalidomide must not be taken if the patient is pregnant, breastfeeding a baby, or able to get pregnant and not using birth controls;

(b) the understanding of potential birth defects;

(c) the warning received by the prescriber regarding said birth defects;

(d) the understanding of the need for at least two forms of contraception prior to, during, and subsequent to thalidomide treatment;

(e) the obligation to undergo a pregnancy test prior to starting thalidomide treatment;

(f) the obligation to undergo a pregnancy test during the thalidomide treatment;

(g) the obligation to discontinue thalidomide treatment and inform the prescriber in the case that the patient is suspected of becoming or being pregnant;

(h) that the patient is not currently pregnant and will not try to become pregnant for at least 4 weeks after the completion of thalidomide treatment;

(i) that thalidomide is solely for the use of the patient herself and must not be shared with any other person;

(j) that the patient has read the information brochure or viewed the information film on thalidomide;

(k) that the blood must not be donated during the thalidomide treatment,

(l) that all of the patient's inquiries regarding thalidomide treatment have been answered by the prescriber; or

(m) the patient's understanding that participation in a survey and patient registry is required during the thalidomide treatment.

50. (Previously Presented) The method of claim 49 further comprising providing the patient, prior to generation of the approval code, with warnings of the side effects associated with administration of thalidomide, wherein said side effects are non-teratogenic side effects.

51. (Previously Presented) The method of claim 49 further comprising obtaining a written authorization by the prescriber prior to generation of the approval code.

52. (Previously Presented) The method of claim 49 wherein the patient is required to use contraception for at least 4 weeks prior to generation of the approval code.

53. (Previously Presented) The method of claim 49 wherein the patient is required to use contraception during thalidomide therapy.

54. (Previously Presented) The method of claim 49 wherein the patient is required to use contraception for at least 4 weeks after discontinuation of thalidomide treatment.

REMARKS

Claims 32-54 are currently pending. Claims 32, 39, 46, and 49 have been amended.

A Final Rejection was mailed on January 8, 2009. The present Reply is being submitted with a Request for Continuing Examination in response thereto.

Applicants wish to thank the examiner and Examiner Astorino for the courtesy of an interview conducted on June 3, 2009 in which the rejections under 35 U.S.C. §§ 101 and 112 were discussed.

35 U.S.C. § 101

Claims 32-54 stand rejected under 35 U.S.C. § 101 for allegedly being directed to non-statutory subject matter. Applicants traverse this rejection. Solely to advance prosecution, claims 32, 39, 46, and 49 have been amended to even more clearly define applicants' invention. For example, the independent claims have been amended to reflect that the presently claimed invention comprises methods for treating a male or female patient suffering from erythema nodosum leprosum with thalidomide, whereby certain steps of the methods (such as registering a prescriber and a pharmacy, generating a prescription approval code, and registering a patient) are performed via a computer. Applicants submit that the claims recite 35 U.S.C. § 101 patentable subject matter and request that the rejection be withdrawn.

35 U.S.C. § 112

Claims 31-54 stand rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. Claims 32, 39, 46, and 49 are allegedly indefinite because it is allegedly unclear how a step of administering thalidomide to a patient is generating a prescription approval code.

Applicants traverse this rejection. Claims 32, 39, 46, and 49 have been amended to recite that upon retrieving a prescription approval code, administering thalidomide to the patient. Moreover, Applicants submit that one skilled in the art would understand the claims to be definite with respect to treating a patient with thalidomide wherein said treatment is permitted only after certain steps are completed and a prescription approval code generated, as provided in the claims. It is clear that the claims encompass a method of controlling a patient's access to certain drugs, namely thalidomide, and that only after certain criteria have

been satisfied is a patient permitted to receive the drug. Applicants respectfully request reconsideration and withdraw of this rejection.

35 U.S.C. § 102

Claims 32-54 stand rejected under 35 U.S.C. § 102(a) as being allegedly anticipated by Transcript, Thalidomide: Potential Benefits and Risks, an open public scientific workshop, Sponsored by National Institutes of Health, Food, and Drug Administration, Centers for Disease Control and Prevention, September 9, 1997 (hereinafter, "Transcript"). Applicants traverse this rejection.

A claim is anticipated "only if each and every element as set forth in the claim is found in a single prior art reference." (*Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987)). Further, "[t]he identical invention must be shown in as complete detail as is contained in the … claim" in the prior art reference. (*Richardson v. Suzuki Motor Co.*, 868 F.2d 1226 (Fed. Cir. 1989) (emphasis added)). This means that the "elements must be arranged as required by the claim." (*In re Bond*, 910 F.2d 831 (Fed. Cir. 1990) (emphasis added); *see also* MPEP § 2131). Applicants respectfully point out that the pending claims cannot be anticipated by the 9/9 Transcript[1] at least because the Transcript does not disclose "identical invention" that was "shown in as complete detail" as recited by the pending claims. (*See Richardson*, *supra*). Further, Applicants respectfully submit that, to the extent that any elements of the claimed methods are disclosed in the Transcript, such elements are not "arranged as required by the [pending claims]." (*Bond*, *supra*).

In this regard, Applicants point out that the Transcript purports to be a word-to-word transcription of an "open public scientific workshop" in which issues associated with making thalidomide available to the public through FDA approval were discussed. By nature, the workshop entailed presentations from various participants on various topics, and many different suggestions, comments, and even debates were made during the workshop. For this reason, to the extent that the Transcript may disclose any elements of the claimed methods, Applicants respectfully point out that such elements are not only broken into pieces and

[1] Applicants make no admission that the Transcript is prior art. Specifically, Applicants respectfully submit that it has not been established that the Transcript was a publication under controlling case law. Further, if it was published, it is unclear when such publication occurred. Nevertheless, the submission made herein demonstrates that the claims are not anticipated by this disclosure, even assuming, *arguendo*, that it is available in prior art under any section of 35 U.S.C. § 102.

scattered all around the entire document in no particular order, but also are in certain instances challenged as not practical or capable of being implemented. Moreover, for some of the elements provided in the Transcript, no consensus among the participants was ever reached.

Consequently, Applicants respectfully submit that the Transcript certainly does not disclose "identical invention" that was "shown in as complete detail" as recited by the pending claims, and the elements are not "arranged as required by the [pending claims]." (*Id.*). Indeed, when read in its entirety, the Transcript cannot disclose the claimed methods because it falls far short of disclosing the coherent and systematic methods recited by the pending claims, which comprise clear and specific steps to be taken in a particular order. Therefore, Applicants respectfully submit that the Transcript cannot anticipate the claimed methods, and thus, respectfully request that the rejection under 35 U.S.C. § 102(a) should be withdrawn.

Moreover, Applicants respectfully point out that the Transcript fails to disclose each and every element of the currently claimed methods. For example, the Transcript does not disclose that via a computer, registering a prescriber and the pharmacy with a distributor of thalidomide. Further, the Transcript does not specifically disclose "providing oral and written warnings of the risk of possible contraception failure and of the need to use barrier contraception when having sexual intercourse with women of child bearing potential" or "providing oral and written warnings of the risk of possible contraception failure and of the need to simultaneous use of two reliable forms of contraception" to patient. Each of these elements is required by the claimed methods. (*See*, *e.g.*, claim 32, 39, 46, and 49). Therefore, Applicants respectfully request that the rejection be withdrawn.

Conclusion

The foregoing represents a *bona fide* attempt to advance the present case to allowance. Applicants submit that the claims are in condition for allowance and an early Notice of Allowance is respectfully requested.

If the Examiner believes that a telephone conference would expedite prosecution of this application, he is invited to call Ms. Angela Verrecchio at the below telephone number.

DOCKET NO.: CELG-0508 **PATENT**
Application No.: 11/437,551
Office Action Dated: January 8, 2009

Date: June 29, 2009

/Stephanie A. Barbosa/
Stephanie A. Barbosa
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Electronic Patent Application Fee Transmittal

Application Number:	11437551
Filing Date:	19-May-2006
Title of Invention:	Methods for delivering a drug to a patient while restricting access to the drug by patients for whom the drug may be contraindicated
First Named Inventor/Applicant Name:	Bruce A. Williams
Filer:	Stephanie A. Barbosa/Kelly Freels
Attorney Docket Number:	CELG-0508

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Extension - 3 months with $0 paid	1253	1	1110	1110

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Request for continued examination	1801	1	810	810
		Total in USD ($)		**1920**

Electronic Acknowledgement Receipt

EFS ID:	5604650
Application Number:	11437551
International Application Number:	
Confirmation Number:	3533
Title of Invention:	Methods for delivering a drug to a patient while restricting access to the drug by patients for whom the drug may be contraindicated
First Named Inventor/Applicant Name:	Bruce A. Williams
Customer Number:	23377
Filer:	Stephanie A. Barbosa/Kelly Freels
Filer Authorized By:	Stephanie A. Barbosa
Attorney Docket Number:	CELG-0508
Receipt Date:	29-JUN-2009
Filing Date:	19-MAY-2006
Time Stamp:	14:35:49
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$1920
RAM confirmation Number	775
Deposit Account	233050
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Request for Continued Examination (RCE)	1267102_1.PDF	1069628 b71a333e15fcc6000f5d8158a90f9ae4a44a2fa2	no	3
Warnings:					
Information:					
2	Extension of Time	1267113_1.PDF	436562 1647d1420eace780af659213fb9cd9ae15962dd6	no	2
Warnings:					
Information:					
3		1283007_1.PDF	138383 99e78ca4c893b0cfcdb19639d5064407b161f4f4	yes	13

Multipart Description/PDF files in .zip description

Document Description	Start	End
Amendment Submitted/Entered with Filing of CPA/RCE	1	1
Claims	2	9
Applicant Arguments/Remarks Made in an Amendment	10	13

Warnings:					
Information:					
4	Fee Worksheet (PTO-875)	fee-info.pdf	32317 4165db07ae36d9e519bda438e4f9278766ed577b	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	1676890	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/06 (07-06)
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PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 11/437,551	Filing Date 05/19/2006	☐ To be Mailed

APPLICATION AS FILED – PART I

	(Column 1)	(Column 2)	SMALL ENTITY ☐		OR	OTHER THAN SMALL ENTITY	
FOR	NUMBER FILED	NUMBER EXTRA	RATE ($)	FEE ($)		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT	06/29/2009	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 23	Minus	** 24	= 0	X $ =		OR	X $52=	0
	Independent (37 CFR 1.16(h))	* 4	Minus	***5	= 0	X $ =		OR	X $220=	0
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	0

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =		OR	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =		OR	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

Legal Instrument Examiner:
/Dorretta Brooks/

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/437,551	05/19/2006	Bruce A. Williams	CELG-0508	3533

23377 7590 09/09/2009

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EXAMINER	
ASTORINO, MICHAEL C	
ART UNIT	**PAPER NUMBER**
3769	

MAIL DATE	DELIVERY MODE
09/09/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	11/437,551	WILLIAMS ET AL.	
	Examiner	Art Unit	
	Michael C. Astorino	3769	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges the response filed on June 29, 2009.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 32-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Transcript, Thalidomide: Potential Benefits and Risks, an open public scientific workshop, Sponsored by National Institutes of Health, Food and Drug Administration, Centers for Disease Control and Prevention, September 9, 1997 (Hereinafter Transcript) and Mayaud et al. WO 96/13790 (provided in applicants IDS and hereinafter Mayaud).

It is the Examiner's position that the Transcript reference teaches all the claimed limitations. As further support for this position, Examiner relies upon, as extrinsic evidence, Guide to CLOZARIL Patient Monitoring Service (provided in the Applicant's IDS and

hereinafter Clozaril Guide) and Pregnancy Prevention Program for Women on Accutane (provided in the Applicant's IDS and hereinafter Accutane PPP), that were referenced by the transcript in the following passages:

> "Although we've received both positive and negative feedback about these suggestions on dispensing, the last two stimulated the most discussion, mainly pertaining to the idea that the pharmacist would also be a gatekeeper for thalidomide, and in some ways serve as the ultimate control over who receives the drug. This is not an idea without precedent. **For at least one drug, Clozaril, dispensing cannot be done unless the pharmacist is presented documentation of requisite laboratory results.**
>
> As an aside, it was encouraging to learn at the FDA meeting last Friday that Celgene will include the patient's diagnosis in **their proposed registry**, and would be able to monitor this data to limit inappropriate or trivial use of thalidomide.
>
> . . . the **Roche pregnancy program for women on Accutane, was a good starting point** . . ."

The only limitations not expressly met by the Transcript reference are the ones regarding the use of a computer to register the prescriber and the pharmacy, and generating the prescription via a computer so that it is received by the Pharmacy before the thalidomide is distributed. However Mayaud, a reference in an analogous art, discloses a computer based prescription system where the prescription is sent automatically from the doctor to the pharmacy (Mayaud Abstract and page 35, lines 13-17). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the invention described in the Transcript with a computer based prescription system taught by Mayaud because Mayaud teaches that using such an automated computer implemented system makes possible significant improvement in the

quality of prescriptions and significantly reduces prescription costs for patients (Mayaud page 7, lines 9-14).

Response to Arguments

Applicant's arguments with respect to claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Astorino whose telephone number is (571)272-4723. The examiner can normally be reached on Monday-Friday, 10:30AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Henry Johnson can be reached on 571-272-4726. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael C. Astorino/
Primary Examiner, Art Unit 3769

September 8, 2009

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	11437551	WILLIAMS ET AL.
	Examiner	Art Unit
	Michael Astorino	3736

SEARCHED

Class	Subclass	Date	Examiner
600	300-301	4/08	MA
128	920	4/08	MA
705	2-4	4/08	MA
235	375	4/08	MA

SEARCH NOTES

Search Notes	Date	Examiner
IDS	4/08	MA
See parent cases	4/08	MA
EAST Inventor Search	4/08	MA
STIC Search to Find sept 1997 Transcript	4/08	MA
Spoke with TQUAS(s) regarding 101 rejection	4/08	MA
West Search Timed out, lost class and text search	4/08	MA
STIC Search	December 2008	SN
Spoke with TQAS regarding 101 and 112 2nd rejections	December 2008	SN
EAST Text Search Updated	December 2008	SN
See 11104103, and applied prior art	9/09	MA

INTERFERENCE SEARCH

Class	Subclass	Date	Examiner

/S. N./ Examiner.Art Unit 3769	

DOCKET NO.: CELG-0508 **PATENT**
Application No.: 11/437,551
Office Action Dated: September 9, 2009

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **Bruce A. Williams and Joseph K. Kaminski**	Confirmation No.: **3533**
Application No.: **11/437,551**	Group Art Unit: **3769**
Filing Date: **May 19, 2006**	Examiner: **Michael C. Astorino**

For: **Methods For Delivering A Drug To A Patient While Restricting Access To The Drug By Patients For Whom The Drug May Be Contraindicated**

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

REPLY PURSUANT TO 37 CFR § 1.111

In response to the Official Action dated **September 9, 2009**, reconsideration is respectfully requested in view of the amendments and/or remarks as indicated below:

☐ **Amendments to the Specification** begin on page of this paper.

☒ **Amendments to the Claims** are reflected in the listing of the claims which begins on page 2 of this paper.

☐ **Amendments to the Drawings** begin on page of this paper and include an attached replacement sheet.

☒ **Remarks** begin on page 10 of this paper.

☐ **Request For Refund** submitted herewith.

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claims 1-31 (Canceled).

32. (Previously Presented) A method of treating a male patient, suffering from erythema nodosum leprosum, with thalidomide, permitting prescriptions for thalidomide to be filled by a pharmacy only after the pharmacy has retrieved an approval code for the prescription, wherein the generation of the prescription approval code comprises the following steps:

(a) via a computer, registering a prescriber and the pharmacy with a distributor of thalidomide;

(b) determining whether the patient is able to understand and reliably carry out instructions;

(c) upon determination that the patient is able to carry out the instructions, providing oral and written warnings of the hazard of taking thalidomide and exposing fetus to the drug;

(d) further providing oral and written warnings of the risk of possible contraception failure and of the need to use barrier contraception when having sexual intercourse with women of child bearing potential;

(e) obtaining acknowledgement of said warnings from the patient;

(f) registering the patient with the distributor; and

(g) upon obtaining the acknowledgement and registration, generating via a computer the prescription approval code to be retrieved by the pharmacy before the prescription is filled; and

upon retrieving a prescription approval code, administering thalidomide to the patient.

33. (Previously Presented) The method of claim 32, wherein the acknowledgement requires the patient's acknowledgement of one or more of the following:

(a) the understanding that thalidomide must not be taken if unprotected sex cannot be avoided;

(b) the understanding of potential birth defects;

(c) that the patient has been advised of the need for barrier contraception by the prescriber;

(d) the obligation to inform the prescriber if the patient's sexual partner is suspected of becoming or being pregnant;

(e) that thalidomide is solely for the use of the patient himself and must not be shared with any other person;

(f) that the patient has read the information brochure or viewed the information film on thalidomide;

(g) that the semen or blood must not be donated during the thalidomide treatment;

(h) that all of the patient's inquiries regarding thalidomide treatment have been answered by the prescribing physician; or

(i) the patient's understanding that participation in a survey and patient registry is required during the thalidomide treatment.

34. (Previously Presented) The method of claim 32 further comprising providing the patient, prior to generation of the approval code, with warnings of the side effects associated with administration of thalidomide, wherein said side effects are non-teratogenic side effects.

35. (Previously Presented) The method of claim 32 further comprising obtaining a written authorization by the prescriber prior to generation of the approval code.

36. (Previously Presented) The method of claim 32, wherein the prescription approval code is retrieved from a computer readable storage medium.

37. (Previously Presented) The method of claim 32, wherein the acknowledgement is a written informed consent.

38. (Previously Presented) The method of claim 37, wherein the written informed consent is registered in the medium prior to generation of the prescription approval code.

39. (Currently Amended) A method of treating a female patient, suffering from erythema nodosum leprosum, with thalidomide, permitting prescriptions for thalidomide to be filled by a pharmacy only after the pharmacy has retrieved an approval code for the prescription, wherein the generation of the prescription approval code comprises the following steps:

(a) via a computer, registering a prescriber and the pharmacy with a distributor of thalidomide;

(b) determining whether the patient is able to understand and reliably carry out instructions;

(c) upon determination that the patient is able to carry out the instructions, determining whether the patient is of child bearing potential;

(d) upon determining that the patient is of child bearing potential, providing oral and written warnings of the hazard of taking thalidomide and exposing fetus to the drug;

(e) further providing oral and written warnings of the risk of possible contraception failure and of the need ~~to~~ for simultaneous use of two reliable forms of contraception;

(f) obtaining acknowledge of said warnings from the patient;

(g) determining, prior to the scheduled beginning of the thalidomide therapy, whether the patient is pregnant;

(h) registering the patient with the distributor; and

(i) generating via a computer the prescription approval code to be retrieved by the pharmacy before the prescription is filled; and

upon retrieving the prescription approval code, administering thalidomide to the patient.

40. (Previously Presented) The method of claim 39, wherein the acknowledgement requires the patient's acknowledgement of one or more of the following:

(a) the understanding that thalidomide must not be taken if the patient is pregnant, breastfeeding a baby, or able to get pregnant and not using birth controls;

(b) the understanding of potential birth defects;

(c) the warning received by the prescriber regarding said birth defects;

(d) the understanding of the need for at least two forms of contraception prior to, during, and subsequent to thalidomide treatment;

(e) the obligation to undergo a pregnancy test prior to starting thalidomide treatment;

(f) the obligation to undergo a pregnancy test during the thalidomide treatment;

(g) the obligation to discontinue thalidomide treatment and inform theprescriber in the case that the patient is suspected of becoming or being pregnant;

(h) that the patient is not currently pregnant and will not try to become pregnant for at least 4 weeks after the completion of thalidomide treatment;

(i) that thalidomide is solely for the use of the patient herself and must not be shared with any other person;

(j) that the patient has read the information brochure or viewed the information film on thalidomide;

(k) that the blood must not be donated during the thalidomide treatment;

(l) that all of the patient's inquiries regarding thalidomide treatment have been answered by the prescriber; or

(m) the patient's understanding that participation in a survey and patient registry is required during the thalidomide treatment.

41. (Previously Presented) The method of claim 39 further comprising providing the patient, prior to generation of the approval code, with warnings of the side effects associated with administration of thalidomide, wherein said side effects are non-teratogenic side effects.

42. (Previously Presented) The method of claim 39 further comprising obtaining a written authorization by the prescriber prior to generation of the approval code.

43. (Previously Presented) The method of claim 39, wherein the prescription approval code is retrieved from a computer readable storage medium.

44. (Previously Presented) The method of claim 39, wherein the acknowledgement is a written informed consent.

45. (Previously Presented) The method of claim 44, wherein the informed written consent is registered in the medium prior to generation of the prescription approval code.

46. (Previously Presented) A method of treating a male patient, suffering from erythema nodosum leprosum, with thalidomide, said method comprising permitting prescriptions for thalidomide to be filled by a pharmacy only after the pharmacy has retrieved an approval code for the prescription from a computer readable storage medium, wherein the generation of the prescription approval code comprises the following steps:

(A) registering a prescriber and the pharmacy via a computer in the computer readable storage medium;

(B) determining whether the patient is able to understand and reliably carry out instructions;

(C) upon determination that the patient is able to carry out instructions, providing oral and written warnings of the hazard of taking thalidomide and exposing fetus to the drug;

(D) further providing oral and written warnings of the risk of possible contraception failure and of the need to use barrier contraception when having sexual intercourse with women of child bearing potential;

(E) obtaining informed consent from the patient;

(F) registering the patient via a computer in the computer readable storage medium; and

(G) upon obtaining the informed consent and registration, generating the prescription approval code to be retrieved by the pharmacy before the prescription is filled, wherein said informed consent requires the patient's acknowledgement of one or more of the following:

(a) the understanding that thalidomide must not be taken if unprotected sex cannot be avoided;

(b) the understanding of potential birth defects;

(c) that the patient has been advised of the need for barrier contraception by the prescriber;

(d) the obligation to inform the prescriber if the patient's sexual partner is suspected of becoming or being pregnant;

(e) that thalidomide is solely for the use of the patient himself and must not be shared with any other person;

(f) that the patient has read the information brochure or viewed the information film on thalidomide;

(g) that the semen or blood must not be donated during the thalidomide treatment;

(h) that all of the patient's inquiries regarding thalidomide treatment have been answered by the prescribing physician; or

(i) the patient's understanding that participation in a survey and patient registry is required during the thalidomide treatment; and

upon retrieving the prescription approval code, administering thalidomide to the patient.

47. (Previously Presented) The method of claim 46 further comprising providing the patient, prior to generation of the approval code, with warnings of the side effects associated with administration of thalidomide, wherein said side effects are non-teratogenic side effects.

48. (Previously Presented) The method of claim 46 further comprising obtaining a written authorization by the prescriber prior to generation of the approval code.

49. (Currently Amended) A method of treating a female patient, suffering from erythema nodosum leprosum, with thalidomide, said method comprising permitting prescriptions for thalidomide to be filled by a pharmacy only after the pharmacy has retrieved an approval code for the prescription from a computer readable storage medium, wherein the generation of the prescription approval code comprises the following steps:

(A) registering a prescriber and the pharmacy via a computer in the computer readable storage medium;

(B) determining whether the patient is able to understand and reliably carry out instructions;

(C) upon determination that the patient is able to carry out instructions, determining whether the patient is of child bearing potential;

(D) upon determining that the patient is of child bearing potential, providing oral and written warnings of the hazard of taking thalidomide and exposing fetus to the drug;

(E) further providing oral and written warnings of the risk of possible contraception failure and of the need ~~to~~ for simultaneous use of two reliable forms of contraception;

(F) obtaining informed consent from the patient;

(G) determining, prior to the scheduled beginning of the thalidomide therapy, whether the patient is pregnant;

(H) registering the patient via a computer in the computer readable storage medium; and

(I) generating the prescription approval code to be retrieved by the pharmacy before the prescription is filled; and

upon retrieving the prescription approval code, administering thalidomide to the patient,

wherein said informed consent requires the patient's acknowledgement of one or more of the following:

(a) the understanding that thalidomide must not be taken if the patient is pregnant, breastfeeding a baby, or able to get pregnant and not using birth controls;

(b) the understanding of potential birth defects;

(c) the warning received by the prescriber regarding said birth defects;

(d) the understanding of the need for at least two forms of contraception prior to, during, and subsequent to thalidomide treatment;

(e) the obligation to undergo a pregnancy test prior to starting thalidomide treatment;

(f) the obligation to undergo a pregnancy test during the thalidomide treatment;

(g) the obligation to discontinue thalidomide treatment and inform the prescriber in the case that the patient is suspected of becoming or being pregnant;

(h) that the patient is not currently pregnant and will not try to become pregnant for at least 4 weeks after the completion of thalidomide treatment;

(i) that thalidomide is solely for the use of the patient herself and must not be shared with any other person;

(j) that the patient has read the information brochure or viewed the information film on thalidomide;

(k) that the blood must not be donated during the thalidomide treatment,

(l) that all of the patient's inquiries regarding thalidomide treatment have been answered by the prescriber; or

(m) the patient's understanding that participation in a survey and patient registry is required during the thalidomide treatment.

50. (Previously Presented) The method of claim 49 further comprising providing the patient, prior to generation of the approval code, with warnings of the side effects associated with administration of thalidomide, wherein said side effects are non-teratogenic side effects.

51. (Previously Presented) The method of claim 49 further comprising obtaining a written authorization by the prescriber prior to generation of the approval code.

52. (Previously Presented) The method of claim 49 wherein the patient is required to use contraception for at least 4 weeks prior to generation of the approval code.

53. (Previously Presented) The method of claim 49 wherein the patient is required to use contraception during thalidomide therapy.

54. (Previously Presented) The method of claim 49 wherein the patient is required to use contraception for at least 4 weeks after discontinuation of thalidomide treatment.

REMARKS

Claims 32-54 are pending in the present application. Claims 39 and 49 have been amended to fix grammatical errors. Applicants note with appreciation that the previous rejections under 35 U.S.C. §§ 101, 112, second paragraph, and 102 have been withdrawn.

35 U.S.C. § 103

Claims 32-54 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over "Transcript, Thalidomide: Potential Benefits and Risks, an open public scientific workshop, Sponsored by National Institute of Health, Food and Drug Administration, and Centers for Disease Control and Prevention," September 9, 1997 ("the 9/9 Transcript"), and Mayaud *et al*. WO 96/13790 ("Mayaud"). Applicants respectfully traverse this rejection.

As an initial matter, the Patent Office has not made a *prima facie* showing that the 9/9 Transcript actually is prior art. Specifically, Applicants respectfully submit that it has not been established that the 9/9 Transcript was a publication under controlling case law. Although the 9/9 Transcript purports to report on a workshop ***conducted*** on September 9, 1997, the ***publication date*** of the 9/9 Transcript has not been established. In fact, there does not appear to be any publication date associated with the 9/9 Transcript. Therefore it is unclear when the 9/9 Transcript was publicly available. Since the Patent Office has failed to establish that the 9/9 Transcript is available prior art, the rejection over it should be withdrawn on this basis alone.

Nevertheless, even assuming, *arguendo*, that the 9/9 Transcript is available as prior art under 35 U.S.C. § 103(a), and Applicants do not concede that it is, Applicants submit that the claims are not obvious in view of it.

Obviousness is determined with respect to the claimed invention as a whole. *Robotic Vision Sys., Inc. v. View Eng'g Inc.*, 189 F.3d 1370, 1376 (Fed. Cir. 1999). An appropriate

consideration of this issue is "whether the references, taken as a whole, would have suggested [the] invention to one of ordinary skill [in the relevant art] at the time the invention was made." *In re Merck & Co.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986). Obviousness is generally established by combining the teachings of two or more items of prior art, such as printed publications or issued patents, or by modifying the teachings of one in light of the other. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). For a claim to be obvious from a modification or combination of the prior art, however, the modification or combination, when made, must provide the invention of the claim. *Id.* at 493.

A proper determination of obviousness also requires, however, that there be some reason for the combination or modification of the prior art to have been made in the first instance. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 ("[I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does."). Whether one of ordinary skill in the art would have seen a "benefit" to making the combination or modification is a relevant inquiry. *Id.* at 422. It remains necessary to show "'some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.'" *Id.* at 418 (citing *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)).

One obviousness standard that satisfies the Supreme Court's *KSR* requirement for a "reason" to combine references is that there be a teaching, suggestion, or motivation, from the prior art or elsewhere, to make the combination or modification, and a suggestion of a reasonable expectation of success in doing so. *In re Vaeck*, 947 F.2d at 493; see *KSR*, 550 U.S. at 419 (The "teaching-suggestion-motivation" standard, although not the only test for a

determination of obviousness, is not inconsistent with section 103 and may be useful in the obviousness analysis).

In the present case, the Examiner explicitly has acknowledged on the record that the 9/9 Transcript fails to teach "the use of a computer to register the prescriber and the pharmacy, and generating the prescription via a computer so that it is received by the Pharmacy before the thalidomide is distributed" (Action at 3). The Examiner asserts, however, that the claimed invention would be obvious in view of Mayaud, and argues that one skilled in the art would be motivated to modify the invention described in the 9/9 Transcript with a computer-based prescription system taught by Mayaud. Applicants disagree.

In addition to the lack of teaching identified by the Examiner above, the 9/9 Transcript also fails to teach or disclose other aspects of the claimed invention. As was previously explained in its June 29, 2009 office action response, Applicants identified that, for example, the 9/9 Transcript does not disclose that the prescriber, the pharmacy, and the patient are registered specifically "with a distributor of thalidomide" via a computer. Further, the 9/9 Transcript does not specifically disclose "providing oral and written warnings of the risk of possible contraception failure and the need to use barrier contraception when having sexual intercourse with women of childbearing potential" or "providing oral and written warnings of the risk of possible contraception failure and of the need for simultaneous use of two reliable forms of contraception." These elements are required by the claimed methods. (*See*, *e.g.*, independent claims 32, 39, 46, and 49). These arguments were previously made in response to an anticipation rejection over the 9/9 Transcript. That rejection has been

withdrawn, which indicates that Applicants' arguments clearly were persuasive and fully accepted by the United States Patent & Trademark Office.

Now, relying on Mayaud, the examiner contends that the claimed invention is obvious. But Mayaud fails to teach or suggest at least the elements identified above that are missing from the 9/9 Transcript. Specifically, for example, Mayaud contains no teaching or suggestion of registering a prescriber, pharmacy and patient with a distributor of thalidomide, providing oral and written warnings of the risk of possible contraception failure and the need to use barrier contraception when having sexual intercourse with women of childbearing potential, or the need for simultaneous use of two reliable forms of contraception. For these independent reasons, the reference should be withdrawn.

Next, the 9/9 Transcript actually *teaches away* from the claimed invention. The examiner stated that it is his position that the 9/9 Transcript teaches all of the claimed limitations and in further support for this position, relies on passages of the 9/9 Transcript referring to, *inter alia*, the Accutane PPP that was referenced in the 9/9 Transcript. The examiner then quotes a portion of the transcript discussing Accutane:

"… the Roche pregnancy program for women on Accutane, was a good starting point…" (Action at 3).

But, the full quote explicitly admits that "… the Roche pregnancy program for women on Accutane, was a good starting point ***but was not rigorous enough for a teratogen as potent as thalidomide***" (9/9 Transcript, emphasis added). Based on this, one skilled in the art would not be motivated to emulate the Accutane program for thalidomide and clearly would recognize the need for a more stringent program. But, there is no teaching or

suggestion in the 9/9 Transcript or in Mayaud of how one skilled in the art could modify the Accutane program to arrive at the claimed invention.

Given these shortcomings by both the 9/9 Transcript and Mayaud, the obviousness rejection of claims 32-54 can not stand and should be withdrawn.

In addition, Applicants submit that the claimed invention is not obvious over the 9/9 Transcript because the invention has produced unexpected results. Evidence of unexpected results must be weighed against evidence supporting *prima facie* obviousness in making a final determination of the obviousness of the claimed invention. *Süd-Chemie, Inc. v. Multisorb Techs., Inc.*, 554 F.3d 1001, 1009 (Fed. Cir. 2009); *In re May*, 574 F.2d 1082 (C.C.P.A. 1978). The present invention, as well as the inventions covered by the patents in the family to which the present application claims priority, have enabled the unexpected benefit of safely administering highly hazardous drugs, such as thalidomide, to patients who might not otherwise have access to these drugs.

Before Celgene pioneered the development of a restricted distribution program for thalidomide, thalidomide was banned by the FDA for the U.S. market. In fact, the potential hazards posed by thalidomide were the driving forces behind significant amendments in the early 1960s to the laws governing the approval of drugs in the United States. Amid doubt and skepticism that a program could be designed to safely administer thalidomide, Celgene succeeded where other companies pointedly had failed -- by devising a safe and effective program under which teratogenic drugs may be distributed to persons in need while minimizing (if not entirely eliminating) the risk of fetal exposure to thalidomide. Since the inception of Celgene's S.T.E.P.S.® risk management system, more than 155,000 patients have registered in the program, as well as over 36,000 pharmacies, and 16,500 physicians. Well

more than one million prescriptions for thalidomide have been processed. In a retrospective study conducted by the FDA to assess, *inter alia*, the occurrence of positive pregnancy tests while on thalidomide treatment, the study found that out of 6000 female patients of childbearing potential, only three had true positive pregnancy tests (Ex. 1).[1] The authors recognized the success of the Celgene program and concluded that "[t]he S.T.E.P.S. programme is critical to managing the risks of thalidomide-associated teratogenicty" (*id.*).

In contrast, risk management programs designed by others have not met with the same kinds of success and the FDA has required revisions to these programs, using the Celgene system claimed by the present application as a model. In particular, in November 2004, FDA announced that the risk management program developed by Roche to monitor the distribution of the teratogenic drug isotretinoin (a.k.a., Accutane), would be revamped (Ex. 2).[2] Under Roche's initial risk management program, which was intended to eliminate the use of isotretinoin by pregnant women, the number of pregnant women using isotretinoin actually ***increased*** (*id.*). Roche's revised program, known as iPLEDGE, is modeled after Celgene's program -- the program claimed by the present application (*id.* and Ex. 3).[3] In fact, Roche licensed the Celgene S.T.E.P.S.® portfolio from Celgene in 2004 (Ex. 4).[4] Generic manufactures of isotretinoin, namely Genpharm Inc., Ranbaxy Laboratories Limited, and

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[1] Uhl, K., et al., "Thalidomide use in the U.S.: experience with pregnancy testing in the S.T.E.P.S. programme," Drug Safety 29(4):321-329 (2006).
[2] "Isotretinoin Risk-Management Program to Be Revamped," November 23, 2004 (available at www.ashp.org/import/News/HealthSystemPharmacyNews/newsarticle.aspx?id=1726).
[3] "Briefing Document for iPLEDGE Year One Update," Drug Safety and Risk Management Advisory Committee and the Dermatologic and Ophthalmic Drugs Advisory Committee, Genpharm, et al. (available at www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4311b1-02-ipledge.pdf).
[4] Press Release- Celgene Licenses S.T.E.P.S.(R) Use Patents to Isotretinoin Manufactures for Safe Distribution of Isotretinoin for Treatment of Severe Recalcitrant Nodular Acne, November 24, 2004 (available at www.redorbit.com/news/health/105537/celgene_licenses_stepsr_use_patents_to_isotretinoin_manufacturers_for_safe/index.html).

Barr Laboratories, jointly coordinated with Roche to develop iPLEDGE and each of these companies has licensed the Celgene S.T.E.P.S.® portfolio from Celgene (*id.*).

Roche's failure and Celgene's commercial success must also be considered in the obviousness determination. These facts -- failure by others and commercial success of the invention-- are evidence of secondary considerations of non-obviousness. *Graham v. John Deere Co.*, 383 U.S. 1 (1966); *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538, (Fed. Cir. 1983). The fact that Roche was unable to devise its own effective risk management program, and instead modeled its iPLEDGE program off of Celgene's inventive program (the program claimed by the present application), indicates the non-obviousness of the present invention. For all of the foregoing reasons, the obviousness rejection of claims 32-54 can not stand and should be withdrawn. Therefore, Applicants respectfully request that the rejection be withdrawn.

Conclusion

The foregoing represents a *bona fide* attempt to advance the present case to allowance. Applicants submit that the claims are in condition for allowance and an early Notice of Allowance is respectfully requested.

If the Examiner believes that a telephone conference would expedite prosecution of this application, he is invited to call the undersigned counsel at the below telephone number.

Date: January 19, 2010

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EXHIBIT 1

ORIGINAL RESEARCH ARTICLE

Drug Safety 2006; 29 (4): 321-329
0114-5916/06/0004-0321/$39.95/0

Thalidomide Use in the US

Experience with Pregnancy Testing in the S.T.E.P.S.® Programme

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Abstract

Introduction: In 1998, thalidomide (Thalomid®), a known human teratogen, was approved by the US FDA for the treatment of erythema nodosum leprosum. To prevent fetal exposure to thalidomide, a restricted distribution risk management programme, the System for Thalidomide Education and Prescribing Safety (S.T.E.P.S.®), was implemented. All clinicians, pharmacists and patients who prescribe, dispense and receive thalidomide, respectively, are required to enrol in S.T.E.P.S.®. Sexually active females of childbearing potential must use two methods of birth control before, during and after treatment. These patients must also have a negative pregnancy test within 24 hours before beginning therapy and periodically while on therapy. The objective of this report is to summarise the patterns of thalidomide use and to describe the occurrence of positive pregnancy tests in females of childbearing potential while they were using thalidomide in the S.T.E.P.S.® programme in the US.

Study design/methods: A retrospective review of patients receiving thalidomide within the S.T.E.P.S.® programme from September 1998 to 31 December 2004 to determine the occurrence of positive pregnancy tests whilst on treatment.

Results: Approximately 124 000 (43% female) patients were registered within the S.T.E.P.S.® programme between September 1998 and 31 December 2004. Approximately 6000 patients were females of childbearing potential, representing 5% of all patients and 11% of all female patients. Between 30 July 2001 and 31 December 2004, >88% of thalidomide use was for oncological conditions. There were 72 females of childbearing potential who had positive pregnancy tests. Sixty-nine of these patients had false positive pregnancy tests. Of the remaining three, one woman was pregnant while on thalidomide. This patient had an initial negative test and received thalidomide. Therapy was stopped when she had a positive pregnancy test. This pregnancy resulted in a miscarriage. Two additional patients were determined to be pregnant before receiving thalidomide.

Conclusions: The S.T.E.P.S.® programme is critical to managing the risks of thalidomide-associated teratogenicity. Sustained vigilance among healthcare providers and patients receiving thalidomide is essential to its continued success.

Healthcare providers should be aware of the occurrence of false-positive pregnancy tests in females of childbearing potential receiving thalidomide.

Introduction

Thalidomide first became available in 1956 in West Germany as a sedative-hypnotic agent. By 1960 it had been introduced in 46 countries (excluding the US) and was widely used to treat nausea and vomiting in early pregnancy. An epidemic of phocomelia, an extremely rare congenital abnormality of the limbs, and other associated malformations in an estimated 15 000 babies soon followed.[1] Germany withdrew thalidomide from its market in November 1961 and other countries followed over the next 10 months.

In 1998 the Thalomid® [1] brand of thalidomide (Celgene Corporation, Summit, NJ, USA), was approved by the US FDA to treat erythema nodosum leprosum. Thalidomide is marketed in three countries outside of the US by the Pharmion Corporation through an international licensing agreement with Celgene. These three countries include Australia, New Zealand and Turkey. There are other companies worldwide that market and distribute other dose presentations of thalidomide; not all of these have risk management programmes.

To prevent fetal exposure to thalidomide, a risk management programme, the System for Thalidomide Education and Prescribing Safety (S.T.E.P.S.®), was implemented in the US, and a similar programme was implemented internationally by Pharmion. All clinicians, pharmacists and patients who prescribe, dispense and receive Thalomid®, respectively, are required to enrol in this restricted distribution programme, regardless of the disease that is being treated.[2] The S.T.E.P.S.® programme is an intensive, multi-component, integrated risk management programme that restricts drug use to registered clinicians, pharmacists and patients (figure 1).

The purpose of the present study is to summarise the patterns of thalidomide use in the US and to describe the cases of positive pregnancy tests that have occurred in females of childbearing potential. This report is a summary of the programme review of registered patients receiving Thalomid® in the mandatory S.T.E.P.S.® programme in the US.

Study Design and Methods

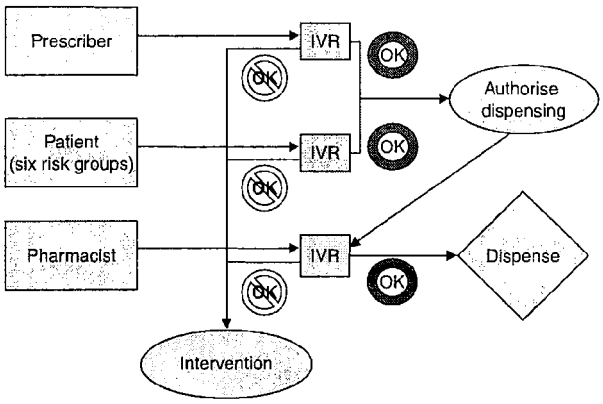
A retrospective review was conducted of patients in the Celgene database who received Thalomid® in S.T.E.P.S.® from September 1998 to 31 December 2004, including a more in-depth review of all patients who had positive pregnancy tests. Patient identifiers were removed for this S.T.E.P.S.® programme evaluation. This research was reviewed and approved by the FDA Research Involving Human Subjects Committee. Descriptive characteristics of all patients with positive pregnancy tests were evaluated including patient demographics, the reason for thalidomide treatment, concomitant medications used and concomitant diseases present.

Females of childbearing potential were defined as postmenarchal women who had not undergone a hysterectomy or who had not been naturally postmenopausal for at least 24 consecutive months (i.e. who have had menses at some time in the preceding 24 consecutive months), in accordance with the Thalomid® product labelling.[3]

All positive pregnancy tests were further evaluated by the patient's healthcare provider using any of the following: serial β-human chorionic gonadotropin (β-hCG) testing, serum hormone testing (e.g. luteinising hormone, follicle-stimulating hormone, estradiol), medical history, physical evaluation, pelvic ultrasound and/or gynaecological consultation according to standard operating procedures adjusted as clinically appropriate. A true-positive pregnancy

1 Thalomid® and S.T.E.P.S.® are registered trademarks of Celgene Corporation. The use of trade names is for product identification purposes only and does not imply endorsement.

test was defined as a positive pregnancy test in a female who was confirmed to be pregnant based upon further evaluation with the aforementioned tests or procedures. A false-positive pregnancy test was defined as a positive pregnancy test in a female who was found not to be pregnant based upon follow-up evaluation. The overall category of false positive pregnancy tests included indeterminate α-hCG test results.



Prescriber: A licensed practitioner and registered in *S.T.E.P.S.*®. The prescriber calls the interactive voice response (IVR) system and responds to a brief series of questions, including the amount of thalidomide (Thalomid®) to be dispensed.

Patient: A person registered within *S.T.E.P.S.*® and able to receive thalidomide. The patient calls the IVR system and responds to a brief series of questions designed to query the patient on procedures to assure safe use of thalidomide.

Pharmacist: A pharmacy registered with *S.T.E.P.S.*® who will dispense thalidomide. The pharmacist calls the IVR system to check if the thalidomide prescription has been authorised (i.e. the physician's and the patient's responses to the IVR queries are in accordance with the parameters for safe use of thalidomide) and enter quantity to be dispensed.

IVR: A telephone-based system used by patients and prescribers to complete required surveys and for pharmacists to receive verification to dispense thalidomide. The IVR verifies that females of childbearing potential are using two methods of birth control, at least one of which is designated as a highly effective method, unless the woman completely abstains from heterosexual sexual contact. The methods of birth control must be initiated 4 weeks prior to beginning thalidomide and the woman must have a negative pregnancy test within 24 hours before the first dose of thalidomide. All females of childbearing potential must have pregnancy tests weekly for the first month of treatment and then monthly until 1 month after stopping therapy. Females with irregular menses must have pregnancy tests every 2 weeks while receiving thalidomide therapy. Any positive qualitative pregnancy test must be followed by a quantitative pregnancy test.

Risk groups: *S.T.E.P.S.*® classifies patients into the following risk categories:
- female child not of childbearing potential
- female child of childbearing potential
- adult female not of childbearing potential
- adult female of childbearing potential
- adult male
- male child.

Authorise dispensing: Upon completion of a patient and/or prescriber survey resulting in no survey intervention, drug can be dispensed by a registered pharmacy.

Dispense: Pharmacy calls the IVR or customer service to dispense thalidomide to a patient.

Intervention: At-risk responses or inappropriate entries in the IVR system result in transfer of the caller to a Celgene *S.T.E.P.S.*® Intervention Specialist for intervention to evaluate and remedy at-risk behaviours when appropriate.

Fig. 1. Schematic of the procedures for prescription authorisation in the System for Thalidomide Education and Prescribing Safety (S.T.E.P.S.®) programme.

The rate of false positive pregnancy tests among females of childbearing potential was calculated for selected reporting period intervals. The numerator comprised the number of false positive pregnancy tests. The denominator comprised the number of pregnancy tests performed during the reporting period intervals. Two-sided 95% confidence intervals were calculated using the normal approximation. The Cochran-Armitage Chi-squared test was used to test for a linear association between time interval (2001, 2002, 2003, 2004) and the rate of false positive pregnancy tests.

Results

Since its approval in 1998 through to 31 December 2004, approximately 726 000 prescriptions for thalidomide were written. Approximately 124 000 patients (57% male and 43% female [table I]) were registered in the S.T.E.P.S.® programme. Approximately 6000 patients were females of childbearing potential, representing 5% of all patients and 11% of all female patients. The prescription of thalidomide in the US by reporting period interval is summarised in table I. The majority of the use of thalidomide (during the period 30 July 2001 to 31 December 2004) is for conditions other than erythema nodosum leprosum, the approved indication, with >88% used for the treatment of oncological conditions (table II).

The number of females of childbearing potential receiving thalidomide has increased since the approval of thalidomide (table I), with a corresponding increase in the number of pregnancy tests (table III). Since females of childbearing potential are required to have pregnancy tests before, during and after therapy, the number of tests is higher than the number of such patients enrolled in S.T.E.P.S.®. Quantitative β-hCG test results were provided for 64 cases, and 80% of these provided the laboratory reference value or ranges for the quantitative test (these data are available as supplementary material from http://www.adisonline.com/drs).

By 31 December 2004, 72 positive pregnancy tests have been reported in the S.T.E.P.S.® programme (69 were ultimately determined to be false positives): four cases in the first 3 years of marketing (September 1998–18 June 2001) and 68 cases from July 2001 to 31 December 2004 (table III). Thalidomide treatment was stopped immediately after a positive pregnancy test, and while test results were being evaluated. Three of the 72 cases represented true pregnancies (case 1, case 2 and case 3). In cases 2 and 3 the mechanism of S.T.E.P.S.® detected pregnancy prior to the patient receiving thalidomide.

Case 1 was a 44-year-old female with "high risk malignant melanoma" that had not responded to multiple prior therapies. She was unable to tolerate oral contraceptives and reported using two barrier methods of contraception. She had a negative pregnancy test on day 8 of her menstrual cycle before starting thalidomide, and had two subsequent negative pregnancy tests during the first month of treatment. On days 35 and 36 of thalidomide therapy she had positive qualitative serum β-hCG tests. Thalidomide therapy was stopped on day 35. On day 42 her quantitative β-hCG level was 1883 mIU/mL (reference value <5 mIU/mL for non-pregnant women). No further quantitative β-hCG results were reported. She had vaginal bleeding on day 63 and ultrasound examination "revealed only blood clots, so it was assumed that the patient passed the foetus" (wording verbatim from MedWatch form). No further follow-up was available.

Case 2 was a 26-year-old female with dermatomyositis who had a positive pregnancy test prior to receiving thalidomide. The patient did not receive thalidomide, but subsequently miscarried.

Case 3 was a 28-year-old female with malignant neoplasm of the vulva who had a positive pregnancy test prior to receiving thalidomide. The patient consulted with her physician and elected to undergo a termination and a tubal ligation. Subsequently, she began thalidomide therapy after it was confirmed that she was not pregnant.

The age range for patients with false-positive pregnancy tests was 12–56 years. These patients received thalidomide for treatment of multiple myeloma (54%), various neoplasms (39%) or other disorders (7%). The total duration of therapy for

Table I. Characteristics of patients receiving thalidomide (Thalomid®) in the S.T.E.P.S.® programme according to reporting period[a]

Risk classification group	Reporting period								Total[b]
	1998[c]	1999[c]	2000[c]	January–29 July 2001[c]	30 July–December 2001[d]	2002[d]	2003[d]	2004[d]	
Males [n (%)]	451 (57.7)	3633 (53.7)	6142 (54.9)	3889 (57.0)	10 555 (56.9)	14 590 (57.4)	15 483 (57.9)	15 889 (58.2)	70 632 (57.2)
Females not of childbearing potential [n (%)]	248 (31.7)	2617 (38.7)	4413 (39.4)	2614 (38.3)	7267 (39.2)	9603 (37.8)	10 009 (37.5)	10 155 (37.2)	46 926 (37.9)
Females of childbearing potential [n (%)]	83 (10.6)	514 (7.6)	633 (5.7)	323 (4.7)	739 (4.0)	1217 (4.8)	1237 (4.6)	1276 (4.7)	6022 (4.9)
Total[d] [n (%)]	782 (100)	6764 (100)	11 188 (100)	6826 (100)	18 561 (100)	25 410 (100)	26 729 (100)	27 320 (100)	123 580 (100)
Thalidomide therapy									
Dose range (mg)	50–1050	50–1400	50–2400	50–2400	50–1400	50–1200	50–1200	50–1200	NA
Mean duration [d (SD)]	35.5 (19.8)	71.1 (66.2)	92.9 (82.5)	101.9 (86.5)	77.65 (444.6)	120.95 (100.4)	126.23 (101.4)	128.90 (102.9)	NA
Mean patient age									
All patients [y (SD)]	53.3 (NA)	57.4 (NA)	60.9 (NA)	62.4 (NA)	66 (14.1)	65 (14.4)	67 (14)	66 (14)	NA
Females of childbearing potential [y (SD)]	NA	NA	NA	NA	42 (9.3)	42 (9.0)	43 (9)	42 (9)	NA

a Represents data from a total of 726 032 prescriptions dispensed.

b Total of percentages may not equal 100% because of rounding.

c Data from Slone Epidemiology Center reports. Some patient demographic information was not available.

d Data from Celgene's S.T.E.P.S.® programme, modified on 30 July 2001. Because the S.T.E.P.S.® programme was modified 30 July 2001, data for the year 2001 is presented in this table for the period January–30 July 2001 and then separately for period 30 July 2001–December 2001.

NA = not available; **SD** = standard deviation; **S.T.E.P.S.®** = System for Thalidomide Education and Prescribing Safety.

Table II. Diagnoses of thalidomide (Thalomid®) recipients by risk classification group (30 July 2001–31 December 2004)[a]

Diagnosis (no. [%] patients)[b]	Males (n = 56 517 [57.66%])	Females not of childbearing potential (n = 37 034 [37.78%])	Females of childbearing potential (n = 4469 [4.56%])	Total (n = 98 020 [100%])
Oncological				
Multiple myeloma	25 988 (26.51)	20 618 (21.03)	1186 (1.21)	47 792 (48.76)
Renal cancer	4200 (4.28)	1567 (1.6)	194 (0.2)	5961 (6.08)
Myelodysplastic syndrome	5051 (5.15)	3145 (3.21)	85 (0.09)	8281 (8.45)
Brain cancer	1759 (1.79)	678 (0.69)	433 (0.44)	2870 (2.93)
Melanoma	2878 (2.94)	1141 (1.16)	466 (0.48)	4485 (4.58)
Prostate malignant neoplasm	3408 (3.48)	0	0	3408 (3.48)
Other neoplasms[c]	7071 (7.2)	5651 (5.77)	870 (0.89)	13 592 (13.87)
Dermatological				
Dermatological diseases	324 (0.33)	503 (0.51)	247 (0.25)	1074 (1.1)
Erythema nodosum leprosum	92 (0.09)	8 (0.01)	10 (0.01)	110 (0.11)
Haematological				
Haematological diseases	1686 (1.72)	1154 (1.18)	68 (0.07)	2908 (2.97)
Infectious diseases				
Infectious diseases	372 (0.38)	247 (0.25)	162 (0.17)	781 (0.8)
Gastrointestinal				
Digestive system/ genitourinary	326 (0.33)	148 (0.15)	105 (0.11)	579 (0.59)
Immunological				
Musculoskeletal/ rheumatological	212 (0.22)	347 (0.35)	230 (0.23)	789 (0.8)
Other	3050 (3.21)	1827 (1.86)	413 (0.42)	5390 (5.5)

a Data on diagnosis from October 1998 to July 2001 are not available.

b Total of percentages may not equal 100% because of rounding.

c Other neoplasms include colorectal, bladder/urethra, liver and other not specified neoplasms.

females of childbearing potential with false positive or indeterminate pregnancy test results ranged from <1 month to 34 months. The duration of treatment at the time of the first false positive pregnancy test in patients receiving thalidomide ranged from 4 days to 17 months. Fifteen of 69 patients had positive pregnancy tests that were determined to be false positive pregnancy tests before thalidomide therapy was initiated. For 68 of 69 patients, β-hCG levels were <350 mIU/mL. One patient with choriocarcinoma, a disease that is expected to produce high concentrations of β-hCG,[4] had levels >350 mIU/mL.

Discussion

The S.T.E.P.S.® programme is a risk management programme designed to prevent fetal exposures to thalidomide. S.T.E.P.S.® is an intensive, multi-component, integrated risk management programme that restricts drug use to registered clinicians, pharmacists and patients. Any suspected fetal exposure to thalidomide (either in female patients or female partners of male patients) in S.T.E.P.S.® participants must be reported immediately to the US FDA and Celgene.[5]

In accordance with the S.T.E.P.S.® programme, sexually active females of childbearing potential must use two appropriate methods of contraception simultaneously to prevent pregnancy for 4 weeks before, during and for 4 weeks following treatment with thalidomide. Appropriate methods of contraception include at least one highly effective method (e.g. intrauterine device, hormonal contraception,

Table III. Thalidomide (Thalomid®) prescriptions and pregnancy tests for females of childbearing potential

	1998–29 July 2001[a]	30 July–December 2001[b]	2002[b]	2003[b]	2004[b]
Prescriptions dispensed (n)	NA	2105	6517	7189	7978
Pregnancy tests (n)	NA	2195	6673	7822	8243
False-positive tests (n)[c]	5	6	20	68	82
Rate of false-positive tests[d] (95% CIs)	NA	0.27% (0.06, 0.49)	0.30% (0.17, 0.43)	0.87% (0.66, 1.08)	0.99% (0.78, 1.21)

a Data from Slone Epidemiology Center Reports.

b Data from Celgene's modified S.T.E.P.S.® programme effective from 30 July 2001.

c The number of false positive pregnancy tests is in excess of the number of cases of false positive pregnancy tests (n = 69) because some patients had more than one positive test result.

d False-positive pregnancy tests divided by number of pregnancy tests. The p-value from the Cochran-Armitage trend test was 0.7914 (Chi-squared [1 degree of freedom] = 0.0700), which indicates a non-significant relationship between year and the false-positive rate.

NA = not available; **S.T.E.P.S.®** = System for Thalidomide Education and Prescribing Safety.

tubal ligation or partner's vasectomy) and one additional effective method (e.g. latex condom, diaphragm or cervical cap). The aforementioned methods of pregnancy prevention must be used unless continuous complete abstinence from heterosexual sexual contact is the chosen method of pregnancy prevention. Females that may become pregnant and postmenarchal women who have not undergone a surgical menopause or who have not been postmenopausal naturally for at least 24 consecutive months (i.e. who have had menses at some time in the preceding 24 consecutive months) are considered to be females of childbearing potential in the S.T.E.P.S.® programme.

All patients agreed to comply with the methods of pregnancy prevention in S.T.E.P.S.®. Despite this, there have been infrequent reports regarding patient difficulties with complying with two forms of contraception. For female patients, one woman reported using two barrier methods, one woman reported that she had a tubal ligation and was not using another method and two women reported missing a dose of birth control pills. Ten male patients reported not using a condom.

According to S.T.E.P.S.®, females of childbearing potential must also have periodic pregnancy testing. Such patient must have a pregnancy test (sensitivity of at least 50 mIU/mL) performed within the 24 hours prior to beginning thalidomide therapy. Pregnancy testing should occur weekly during the first 4 weeks of use, then at 4-week intervals in women with regular menstrual cycles or every 2 weeks in women with irregular menstrual cycles. Pregnancy testing should also be done if any female of childbearing potential misses her period or has any abnormality in menstrual bleeding. Any positive qualitative urine pregnancy test is followed by a more sensitive qualitative serum and/or a quantitative serum pregnancy test.

Thalidomide is present in the semen of male patients receiving the drug. Male patients receiving thalidomide who are sexually active with women who are or could become pregnant must always use a latex condom during any sexual contact, even if the male patient has undergone a successful vasecto-

my. However, the risk to the fetus from exposure to thalidomide in the semen is unknown. To date there have been 18 reports to the S.T.E.P.S.® programme of pregnancies in female partners of male patients taking thalidomide: 14 normal newborns, one ectopic pregnancy termination and three pregnancies with limited or no available follow-up information.

The initial design of the S.T.E.P.S.® programme retrospectively identified patient behaviours providing a risk of fetal exposure to thalidomide; therefore, procedural changes to the S.T.E.P.S.® programme were instituted in July 2001. These changes were designed to ensure that results from the required pregnancy tests were documented and linked to prescription activation and dispensing through an interactive voice response (IVR) system or via customer service prior to dispensing thalidomide. When an 'at risk' behaviour (e.g. a pending, outdated or positive pregnancy test result) is identified using the IVR system, the caller is transferred to a Celgene S.T.E.P.S.® Intervention Specialist.[3] On average, 5% of surveys require an intervention, verification or clarification of a patient or prescriber response prior to dispensing thalidomide.[3] The majority of all issues are addressed within 24 hours of identification by the IVR system. Thalidomide is not given if there is a known non-compliance issue.

Since the approval of Thalomid® in the US, only three women in the S.T.E.P.S.® programme have been identified as becoming pregnant: one after thalidomide was initiated and two at the time of enrolment but before the initiation of treatment with thalidomide. There were 69 other females of childbearing potential who had false-positive pregnancy tests after enrolling in S.T.E.P.S.® (please see http://www.adisonline.com/drs for individual patient information). Women who have false-positive β-hCG pregnancy tests usually have levels that remain consistently low,[6,7] as was seen in thalidomide users in this case series. Early pregnancy loss is associated with rapidly falling β-hCG levels;[8,9] therefore, the persistence of low β-hCG levels in the 69 cases is not suggestive of a true pregnancy that underwent early loss after exposure of the developing conceptus to thalidomide.

The frequency of false-positive pregnancy tests as a percentage of pregnancy tests performed (0.27–0.99%) has remained stable since the beginning of the modified S.T.E.P.S.® programme that was initiated in July 2001 (table III), and the observed rate of false-positive pregnancy tests is comparable to estimated rates of false-positive pregnancy tests in the general population of females of childbearing potential.[7] Pregnancy rates among comparable females not taking thalidomide were not available for comparison. The occurrence and general management of false-positive pregnancy tests are reviewed elsewhere.[10] Serial pregnancy tests, specialised laboratory tests, pelvic ultrasound or medical consultation can help distinguish between true- and false-positive pregnancy tests. In this series, nine cases had further clinical evaluation for positive pregnancy tests beyond repeat β-hCG testing: six had ultrasound studies, three had CT scans and one had further laboratory evaluation.

The institution of the IVR system in July 2001 was designed to identify patients exhibiting behaviours providing risk for fetal exposure and to remedy those behaviours prior to dispensing thalidomide. The continued ongoing evaluation of S.T.E.P.S.® will be essential to evaluate the programme's performance and to guide future refinements to the programme, in order for it to achieve its objectives.

Even with the use of thalidomide for a variety of medical conditions, the majority of which were for haematological malignancies (e.g. multiple myeloma) and solid organ tumours, the amount of thalidomide used in the US is relatively small. Similar risk management programmes for other drugs that have demonstrated adverse risks associated with fetal exposure, such as isotretinoin,[11] have been developed and implemented by drug manufacturers. The Celgene S.T.E.P.S.® programme has been licensed to several other drug manufacturers with the regulatory involvement of the FDA, for the increased surveillance and monitoring of physicians, pharmacists and patients, to prevent fetal ex-

posure to drugs. The vigilance of physicians, pharmacists, patients, Celgene and the FDA has contributed to the success of S.T.E.P.S.® in preventing pregnancy in females receiving thalidomide.

Conclusions

The S.T.E.P.S.® programme has been successful in preventing fetal exposure to thalidomide. Of the 6022 females of childbearing potential registered in the S.T.E.P.S.® programme, one patient became pregnant while receiving the drug and two additional patients were identified as pregnant and were not permitted to start thalidomide treatment. This 'real time' risk management programme may be a useful model to prevent exposure of pregnant women to other drugs that are known human teratogens or that are suspected to be teratogenic (based upon drug class or findings in experimental animal studies). Because important clinical decisions may be made on the basis of the results of pregnancy testing, clinicians using thalidomide must remain vigilant in evaluating every female with a positive pregnancy test until pregnancy is either confirmed or ruled out. Both the FDA and Celgene remain committed to preventing fetal exposure to thalidomide.

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EXHIBIT 2

American Society of Health-System Pharmacists®
TOGETHER WE MAKE A GREAT TEAM

Isotretinoin Risk-Management Program to Be Revamped

KATE TRAYNOR

BETHESDA, MD, 23 November 2004—The Food and Drug Administration (FDA) today announced changes to the risk management program for isotretinoin that will be implemented next July with the goal of eliminating use of the teratogenic drug by pregnant women.

Isotretinoin is indicated for the treatment of severe recalcitrant nodular acne and has been marketed in this country since 1982.

The previous risk management program—System to Manage Accutane Related Teratogenicity (SMART)—was implemented in April 2002 by Roche Pharmaceuticals, which markets Accutane, the innovator isotretinoin product. Generic versions of the drug entered the market in late 2002, with each manufacturer providing the drug through separate risk management programs modeled after SMART.

Under SMART, which remains in effect until the new risk management system is in place, valid prescriptions for isotretinoin must bear a yellow sticker signifying that the woman presenting the prescription has twice tested negative for pregnancy before initiating therapy. Stickers are provided by isotretinoin manufacturers to physicians who register to become authorized prescribers of the drug. A new prescription, with a new sticker, is required for each 30-day supply of the drug.

To meet its goals, SMART relies on unauthorized physicians to refrain from prescribing isotretinoin and pharmacists to refuse to fill prescriptions unless they bear the sticker. Another key element is that authorized physicians must not affix the sticker to a woman's prescription unless a properly timed negative pregnancy test result was obtained. Roche revealed at a February 2004 FDA advisory committee meeting that compliance with these elements of SMART has not been universal.

In fact, Roche found that documented cases of pregnancy among isotretinoin users actually increased after SMART was implemented. In all, Roche received 150 case reports of pregnancy before SMART implementation and 183 afterward. The company attributed the increased number of cases to better reporting but suggested revisions to SMART that would help the program reach its intended goal.

The revised program requires that patients and pharmacies, as well as physicians, register with a centralized clearinghouse that will be responsible for authorizing prescriptions for isotretinoin. The single registry will replace the manufacturer-specific registries that currently allow physicians to prescribe the drug.

FDA stated that patients and physicians who have been fully compliant with SMART will not encounter substantial new difficulties obtaining the drug under the revised program.

The registry is modeled after Celgene Corp.'s System for Thalidomide Education and Prescribing Safety (STEPS) risk management program for thalidomide, a potent teratogen. STEPS is a patented system that uses a voice-activated telephone system for prescribers, patients, and pharmacists to enter and verify information related to the prescribing and dispensing of thalidomide. Dispensing occurs only after the pharmacist has received an authorization code from the system.

FDA stated that issues related to Celgene's patenting of the STEPS methodology were recently resolved among the approved isotretinoin manufacturers and Covance Inc., which will run the new registry.

A press release issued today by Covance stated that the new risk-management program "will require [pregnancy] test results from certified laboratories" to be entered into the system and that women will no longer be able to perform their monthly pregnancy testing at home or at a physician's office.

FDA stated that when the registry denies an authorization to fill the prescription, the patient's physician would be responsible for communicating the reason for the denial to the patient. The agency stated specifically that the physician is responsible for telling a woman if a pregnancy test result comes back positive.

Isotretinoin manufacturers are responsible for establishing and maintaining the clearinghouse, according to FDA. Drug makers will also monitor movement of their products through unauthorized distribution routes, including the Internet.

FDA stated that its announcement about the strengthening of the risk-management program was tied to issues surrounding Celgene's patents and was unrelated to "political pressure" about drug safety.

Isotretinoin is one of five drugs that David Graham, associate director for science in the FDA's Office of Drug Safety, last week described as too risky to remain on the market. Graham made the comment while testifying before the Senate Finance Committee investigating the recent market withdrawal of Vioxx, Merck's rofecoxib product, which has been blamed for cardiovascular events and deaths.

EXHIBIT 3

DRUG SAFETY AND RISK MANAGEMENT ADVISORY COMMITTEE

DERMATOLOGIC AND OPHTHALMIC DRUGS ADVISORY COMMITTEE

BRIEFING DOCUMENT

FOR

iPLEDGE YEAR ONE UPDATE

AMNESTEEM® produced by Genpharm Inc; distributed by Mylan Pharmaceuticals

SOTRET® produced by Ranbaxy Laboratories Limited

Claravis™ produced by Barr Laboratories

ACCUTANE® produced by Roche Laboratories Inc

AVAILABLE FOR PUBLIC DISCLOSURE WITHOUT REDACTION

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1. EXECUTIVE SUMMARY

1.1 Background

The isotretinoin pregnancy risk management program, iPLEDGE, is a computer-based, restrictive distribution program and pregnancy registry which provides a closed-loop system for prescribing, dispensing, and distributing isotretinoin. The program's goals are to ensure that no woman starts isotretinoin therapy if she is pregnant and that no woman on isotretinoin therapy becomes pregnant during therapy and for 1 month after discontinuing isotretinoin treatment. iPLEDGE was developed by the isotretinoin sponsors (Barr Laboratories, Genpharm Inc., Mylan Pharmaceuticals Inc., Ranbaxy Laboratories Limited, and Roche Laboratories Inc.) in collaboration with the Food and Drug Administration (FDA) during 2004 and 2005. The iPLEDGE program began accepting patient registrations on December 30, 2005 and became mandatory as of March 1, 2006.

Key elements of iPLEDGE include:

- Single, centralized program for all isotretinoin products
- Registration of all healthcare professionals prescribing or dispensing isotretinoin
- Mandatory, monthly, laboratory-based, pregnancy tests for females of childbearing potential before each new prescription is authorized
- Mandatory, monthly, patient-education questions via an interactive web/phone based system
- A centralized pregnancy registry with root cause analysis for all pregnancies
- A technical infrastructure to support the above registrations, collection of laboratory pregnancy test results, and verification of patient qualifications

The remainder of this document reviews components of the iPLEDGE program, summarizes the changes implemented in the program after launch and the plan for additional program changes to meet the stakeholder needs for efficiency, and provides data from the first year of iPLEDGE (March 1, 2006 through February 28, 2007) including user compliance and pregnancies.

1.2 iPLEDGE Year 1 Update

The main highlights from the iPLEDGE Year One update are as follows:

- The iPLEDGE program is a risk management program of unprecedented size and scope with over 189 wholesalers, 42,362 pharmacies, 15,742 prescribers, and 305,366 patients registered during Year One.
- The majority of the recommended stakeholder changes to increase stakeholder efficiency have been or are in the process of being implemented into the program.
- A centralized isotretinoin pregnancy registry was established and data from its first year provide a baseline for subsequent comparisons.
- Educational messages about the need to avoid pregnancy and to use two forms of contraception for 1 month before, during, and 1 month after isotretinoin therapy are

being communicated by prescribers and are reaching female patients of childbearing potential.

- Overall, 137,415 females of childbearing potential were registered during Year One and 91,894 of these patients had an isotretinoin prescription authorized through the iPLEDGE system. A total of 122 pregnancies were reported. The majority of these pregnancies occurred after isotretinoin therapy was initiated. Most pregnancies were associated with contraceptive noncompliance.
- Almost all pregnant and nonpregnant women demonstrated an understanding of both the need to use contraception and the risk of birth defects for isotretinoin-exposed pregnancies.

2. EVOLUTION OF RISK MANAGEMENT INITIATIVES FOR PREGNANCY PREVENTION

Isotretinoin is a human teratogen that is uniquely efficacious for the treatment of severe recalcitrant, nodular acne in patients who are unresponsive to conventional therapy, including systemic antibiotics. The safe use of isotretinoin in women requires that every effort be made to 1) prevent pregnant women from taking isotretinoin; and 2) prevent women of childbearing potential from becoming pregnant 1 month before initiation of isotretinoin therapy, during therapy, and for 1 month after discontinuing isotretinoin treatment.

The innovator isotretinoin drug, ACCUTANE® was introduced to the United States in 1982 with a Category X pregnancy designation, the designation for drugs that must be avoided under all circumstances during pregnancy. Over the years, the strategies to prevent maternal/fetal exposure to isotretinoin have included both warnings in the product label, focused educational materials for prescribers and patients, and risk management programs for pregnancy prevention, the first of which, the Pregnancy Prevention Program, was introduced by Roche in 1988 (Appendix 1). This was followed by an enhanced risk management program, the System to Manage Accutane Related Teratogenicity® (S.M.A.R.T.®) in 2002, which was based in part on data generated from the Pregnancy Prevention Program. Risk management programs with the same components of S.M.A.R.T. were introduced with the approval of generic versions of isotretinoin beginning in November 2002.

On February 26 and 27, 2004, a joint advisory committee meeting was held between the Drug Safety and Risk Management Advisory Committee and the Dermatologic and Ophthalmic Drugs Advisory Committee to discuss the first year results of S.M.A.R.T. The discussion focused on whether changes were necessary to S.M.A.R.T. and its generic equivalents. At this meeting, the sponsors presented a proposal for a single, enhanced isotretinoin pregnancy risk management program, which included mandatory registration of prescribers, patients, and pharmacies, automatic system verification of pregnancy test results, and a centralized pregnancy registry for reporting and follow-up of pregnancies.

Based on the recommendations of the Advisory Committees and the FDA White Paper (issued July 2004), the sponsors developed a unified, mandatory, isotretinoin pregnancy

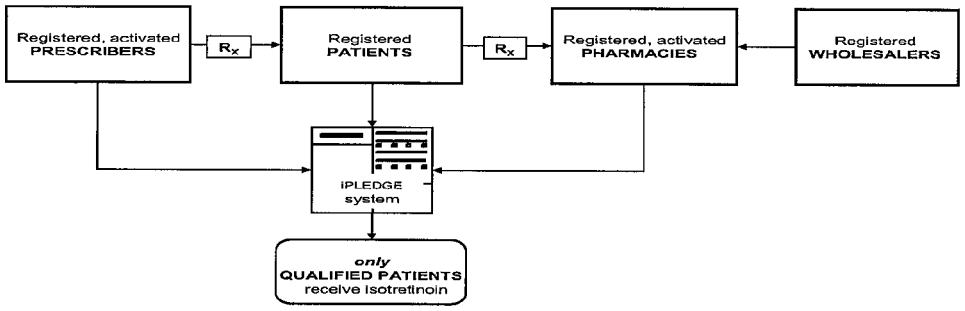
risk management program, iPLEDGE, with a single centralized pregnancy registry to replace all previous isotretinoin risk management programs.

3. iPLEDGE

3.1 Program Overview

The iPLEDGE program is a computer-based, centralized registry of prescribers, patients, pharmacies, and wholesalers, that provides a closed-loop system for prescribing, dispensing, and distributing isotretinoin (Figure 1). The public health goal of the iPLEDGE program is to eliminate fetal exposure to isotretinoin by ensuring that: 1) no female patient starts isotretinoin therapy if pregnant; and 2) no female patient on isotretinoin therapy becomes pregnant.

Figure 1 iPLEDGE System



Key elements of iPLEDGE include:

- Mandatory registration of wholesalers
- Mandatory registration and education of all isotretinoin prescribers
- Mandatory registration of all dispensing pharmacies via a responsible site pharmacist
- Mandatory registration and education of all patients prescribed isotretinoin
- Mandatory, laboratory-based, pregnancy tests for females of childbearing potential prior to authorization for each new prescription
- Mandatory, interactive-educational questions about contraception and birth defects prior to each new prescription for females of childbearing potential
- Authorization for isotretinoin to be dispensed only after a patient has met all iPLEDGE requirements
- A centralized pregnancy registry
- A technical infrastructure to support the above registrations, collection of laboratory pregnancy test results, and verification of patient qualifications

The iPLEDGE program began accepting patient registrations on December 30, 2005 and became mandatory as of March 1, 2006. This document reviews components of the iPLEDGE program, summarizes the changes implemented in the program after launch and the plan for additional program changes to meet the stakeholders needs for efficiency, and provides data from the first year of iPLEDGE (March 1, 2006 through February 28, 2007) including user compliance and pregnancies.

3.2 iPLEDGE Requirements and Processes

iPLEDGE has specific processes and requirements that target all aspects of the isotretinoin prescribing chain which includes wholesalers, prescribers, pharmacies, and patients. Many of these iPLEDGE processes have been designed to address gaps identified in the previous risk management programs for isotretinoin (Table 1). A brief description of the specific iPLEDGE processes and requirements is provided below for each of the iPLEDGE stakeholders.

Table 1 Risk Management Enhancements with iPLEDGE

Gaps Identified From Previous Risk Management Programs	Risk Management Enhancements in iPLEDGE
• Strengthen the verifiable link between pregnancy testing and dispensing of isotretinoin • Reinforce pregnancy testing requirements with patients and prescribers	• Monthly pregnancy tests (either serum or urine) must be conducted in an accredited laboratory (CLIA certified) • Automatic system verification of negative pregnancy test results that are entered by the prescriber before a pharmacist can dispense isotretinoin • A formalized process for following-up with prescribers and patients if expected pregnancy test results are not entered into the system (lost to follow-up procedure)
• Reinforce patient contraception requirements	• Patient and prescriber entries for the primary contraceptive form must match • Patients must answer education questions each month (tailored to the patient's selected methods of contraception)
• Multiple risk management programs for isotretinoin are a source of confusion for patients and prescribers	• Single pregnancy risk management program
• Limited participation with voluntary patient surveys	• Automatic system check to verify patients interact with the system and answer first month questions
• Improve the method for capturing pregnancy reports and the information collected to better evaluate isotretinoin-exposed pregnancies	• A centralized pregnancy exposure registry with root cause analysis for each pregnancy • A formalized process for following-up with prescribers and patients if expected pregnancy test results are not entered into the system (lost to follow-up procedure) to ensure that a potential pregnancy does not go unreported
• Reinforce education of all patients and healthcare providers*	• Mandatory registration and education of all patients prescribed isotretinoin • Automatic system check to verify patient counseling by the prescriber and that the patient answers educational questions correctly each month • Mandatory registration and education for pharmacies

*Mandatory prescriber registration and education, a component of the previous isotretinoin risk management programs, was continued with iPLEDGE.

3.2.1 Wholesalers Process and Requirements

For the purpose of the iPLEDGE program, the term wholesaler refers to wholesaler, distributor, and/or chain pharmacy distributor. To distribute isotretinoin, wholesalers must be registered with iPLEDGE and agree to meet all iPLEDGE requirements for wholesale distribution of isotretinoin products. Wholesalers must register with iPLEDGE by signing and returning the iPLEDGE wholesaler agreement form that affirms they will comply with all iPLEDGE requirements for distribution of isotretinoin. These requirements include:

- Registering prior to distributing isotretinoin and reregistering annually
- Distributing only FDA-approved isotretinoin product
- Shipping isotretinoin only to: 1) wholesalers registered in the iPLEDGE program with the prior written consent from the manufacturer; and 2) pharmacies licensed in the United States that are registered and activated in the iPLEDGE program

On a daily basis, the iPLEDGE system receives any changes in pharmacy status (openings, relocations, closings in the United States) from the National Council for Prescription Drug Programs. iPLEDGE provides to wholesalers a daily update of all registered and activated pharmacies that are eligible to receive isotretinoin shipments. Wholesalers are responsible for checking this list before distributing any isotretinoin.

3.2.2 Prescriber Process and Requirements

To prescribe isotretinoin, the prescriber must be registered and activated with iPLEDGE. Prescribers can register by signing and returning the completed, paper-based, registration form or via the internet. Prescribers can only activate their registration by affirming that they meet and will comply with all iPLEDGE requirements. This process must be completed annually.

To prescribe isotretinoin, the prescriber must:

1) Register each patient in the iPLEDGE program. Female patients of childbearing potential are registered after an initial negative pregnancy test and males and females of nonchildbearing potential are registered at the time of receiving their first isotretinoin prescription.

2) Confirm, before beginning isotretinoin treatment of female patients of childbearing potential and on a monthly basis, that each patient will be counseled to avoid pregnancy by using two forms of contraception simultaneously and continuously or commit to continuous abstinence one month before, during, and one month after isotretinoin therapy. This process was designed to remind prescribers monthly to reinforce the requirements for appropriate isotretinoin risk management.

3) Obtain a signed Patient Information/Informed Consent Form that contains warnings about the potential risks associated with isotretinoin.

4) For female patients of childbearing potential:

- Confirm that, in the prescriber's opinion, the patient can comply with the iPLEDGE requirements.
- Obtain an additional Patient Information/Informed Consent About Birth Defects Form that contains warnings about the risk of potential birth defects if the fetus is exposed to isotretinoin.
- Enter the patient's two chosen forms of contraception each month. This process was designed to confirm the patient's contraceptive choice and that she was counseled and instructed to use two forms of contraception each month.
- Enter monthly results from laboratory-conducted (CLIA-certified) serum or urine pregnancy test. This requirement was designed to reinforce the pregnancy testing requirements with prescribers and to provide a verifiable link between a negative pregnancy test and the dispensing of isotretinoin.

To facilitate the dialogue between prescribers and females of childbearing potential about the iPLEDGE program requirements and to reinforce the educational messages about contraceptive use and the need to avoid pregnancy to female patients of childbearing potential, prescribers are provided with the following educational material:

- *The iPLEDGE Program Guide to Best Practices for Isotretinoin* that includes information on the teratogenic potential of isotretinoin, information on pregnancy testing, and the method to complete a qualified isotretinoin prescription.
- *The iPLEDGE Program Prescriber Contraception Counseling Guide* that includes specific information about effective contraception, the limitations of contraceptive methods, behaviors associated with an increased risk of contraceptive failure and pregnancy, and the methods to evaluate pregnancy risk.

Prescribers are also provided with a DVD with two videos, "Be Prepared, Be Protected" and "Be Aware: The Risk of Pregnancy While on Isotretinoin" that can be shown to the female patients of childbearing potential during the first office visit. Prescribers are also reminded to offer to all female patients of childbearing potential a referral for specialized contraceptive counseling that may be reimbursed by the isotretinoin manufacturer.

3.2.3 Patient Process and Requirements

3.2.3.1 Females of Childbearing Potential

The iPLEDGE pathway for a female of childbearing potential to receive a 30-day supply of isotretinoin is outlined in Figure 2.

Some aspects of iPLEDGE are similar to the previous risk management programs for females of childbearing potential, but are now documented and verified by the iPLEDGE system. For example, females of childbearing potential must have monthly pregnancy tests and must use two forms of contraception 1 month before, during, and 1 month after isotretinoin therapy.

Some of the new requirements with iPLEDGE for females of childbearing potential include patient registration in iPLEDGE and patient monthly interactions with the system

to document her two chosen forms of contraception. Two appropriate forms must be selected or the patient will not be authorized to receive isotretinoin, except where abstinence is selected as the primary method. Additionally, the system verifies that the contraceptives entered into the system by the patient matches that entered by her prescriber.

To facilitate patient-prescriber conversations about the need to avoid pregnancy for 1 month before, during, and 1 month after stopping isotretinoin therapy, and the contraceptive requirements of iPLEDGE, prescribers and female patients of childbearing potential are provided with a series of educational materials. To ensure that the key educational messages in these materials were being communicated and understood, the sponsors had the educational material comprehension tested among a national sample of consumers. Educational material provided to females of childbearing potential includes:

- *The iPLEDGE Program Guide to Isotretinoin for Female Patients Who Can Get Pregnant* that includes a referral program that offers female patients free (reimbursed by the manufacturer if not covered by the patient's health insurance) contraception counseling by a reproductive specialist and a second Patient Information/Informed Consent About Birth Defects form concerning birth defects.
- *The iPLEDGE Program Birth Control Workbook* that includes information on the types of contraceptive methods, the selection and use of appropriate, effective contraception, the rates of possible contraceptive failure, and a toll-free contraception information line.
- A patient educational DVD with the videos "Be Prepared, Be Protected" and "Be Aware: The Risk of Pregnancy While on Isotretinoin". These videos describe the birth defects that may happen if a woman takes any isotretinoin while pregnant and also reviews reasons for contraceptive failure.

In order to qualify to receive her first isotretinoin prescription, a female of childbearing potential must interact with the iPLEDGE system to answer a series of questions to determine if she received the educational material that was to be provided by her prescriber. This component of the iPLEDGE program was designed: 1) to address the limited patient participation seen in the Accutane survey of S.M.A.R.T. and similar surveys sponsored by the generic manufacturers; and 2) to allow for the collection of information on how well the iPLEDGE process is followed. These questions are only asked for the first prescription and include the following:

1. Did your doctor or anyone in your doctor's office tell you that it is important not to become pregnant while taking isotretinoin? (Yes/No)
2. Did you receive the iPLEDGE program isotretinoin educational kit for female patients who can get pregnant? (Yes/No)
   - If yes, did you read
     - The *iPLEDGE Program Guide to Isotretinoin for Female Patients who Can Get Pregnant*? (Yes/No)
     - The *iPLEDGE Program Birth Control Workbook*? (Yes/No)
3. Did you watch the video "Be Prepared, Be Protected" about birth control? (Yes/No)

4. Did you watch the video "Be Aware: The Risk of Pregnancy while on Isotretinoin"? (Yes/No)
5. Did you or anyone in your doctor's office offer to refer you to another healthcare provider for birth control counseling? (Yes/No)
6. From whom did you receive birth control counseling?
   - My doctor
   - Another healthcare provider provided
   - I did not receive birth control counseling

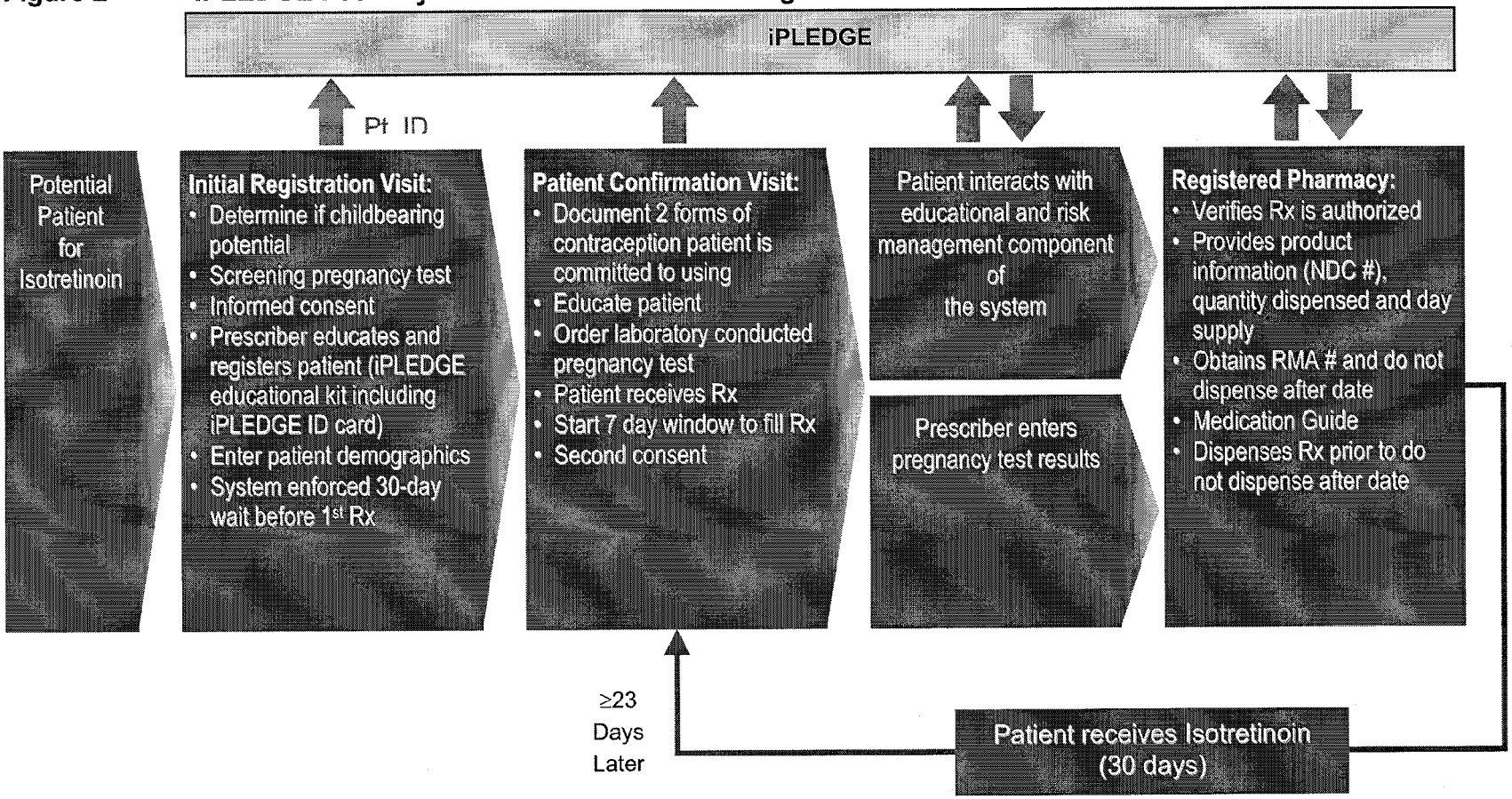
For the first and all subsequent months of isotretinoin therapy, female patients of childbearing potential must also answer a series of questions to demonstrate their understanding of the need to use contraception and the risk of birth defects. These questions can be grouped into the following categories:

- Program steps
- General contraception requirements
- Birth defects and pregnancy
- Safety information (sharing, giving blood)
- Filling a prescription
- Birth control (questions in this category are randomly selected based upon the contraceptive choices entered into the system by the prescriber and the patient)
  - Primary birth control
  - Secondary birth control

Patients must correctly answer one randomly selected question from each category (total of 6 questions). If a question is answered incorrectly, the patient is then presented with a second question from the same category. If this question is answered incorrectly, the patient fails the test and is required to take the test again. For each question that is answered incorrectly, the patient is provided with a specific reference to one of the educational materials to review. There is no time restriction on when the test can be retaken, however, the test must be passed for the isotretinoin prescription to be authorized.

Once all iPLEDGE requirements for females of childbearing potential are met, isotretinoin prescriptions can only be filled and picked up within a defined time window (within 7 days of the prescriber's office visit date). Currently, female patients of childbearing potential may not start the qualification process for another isotretinoin prescription until 23 days after the end of their 7-day window, whether a prescription was filled or not (see Section 3.6).

Figure 2 **iPLEDGE Pathway for Females of Childbearing Potential**



RMA=Risk Management Authorization; NDC=National Drug Code

3.2.3.2 Males and Females of Nonchildbearing Potential

The primary change for males and females of nonchildbearing potential compared to the previous isotretinoin risk management programs is registration in iPLEDGE. These patients are not required to interact with the system as a part of their isotretinoin treatment and participation in iPLEDGE.

All males and females of nonchildbearing potential continue to have monthly office visits, complete the informed consent process, and only receive up to a 30-day supply of isotretinoin with no refills. This requirement is the same as with the previous isotretinoin risk management programs.

Males and females of nonchildbearing potential must also fill and pickup their isotretinoin prescriptions within 7 days of the prescriber's office visit, but can start the qualification process over immediately at the end of their 7-day window, if a prescription was not filled (see Section 3.5).

The iPLEDGE Program Guide to Isotretinoin for Male Patients and Female Patients Who Cannot Get Pregnant is provided to males and female patients of nonchildbearing potential. This booklet includes information about male reproduction and a warning not to share isotretinoin with others or to donate blood during isotretinoin therapy and for 1 month following discontinuation of isotretinoin.

3.2.4 Pharmacy Process and Requirements

Isotretinoin can only be dispensed by licensed pharmacies in the United States that are registered and activated with iPLEDGE. Pharmacies are the key to ensuring that the patient does not obtain isotretinoin unless all iPLEDGE requirements have been fulfilled. Each pharmacy must identify a responsible site pharmacist who must register the pharmacy by signing and returning the completed registration form. After registration, the responsible site pharmacist can only activate the pharmacy registration by affirming that all pharmacists meet and will comply with all iPLEDGE requirements. This process must be repeated annually.

To ensure that isotretinoin is dispensed only to patients who are registered in iPLEDGE and are authorized to receive product, a pharmacist must:

1) be trained by the responsible site pharmacist about the iPLEDGE program requirements.

2) obtain authorization from the iPLEDGE program via the internet (www.ipledgeprogram.com) or telephone (1-866-495-0654) for every isotretinoin prescription. Authorization signifies that the patient has met all program requirements and is qualified to receive isotretinoin.

3) write the Risk Management Authorization number on the prescription.

Isotretinoin must only be dispensed in no more than a 30-day supply with an isotretinoin Medication Guide within 7 days of the prescriber's office visit. Automatic refills for isotretinoin are not allowed.

Pharmacists are provided with *The iPLEDGE Program Pharmacist Guide for Isotretinoin* that includes information about the teratogenic potential of isotretinoin and the method to obtain authorization to dispense an isotretinoin prescription.

3.3 Patients Lost to Follow-up

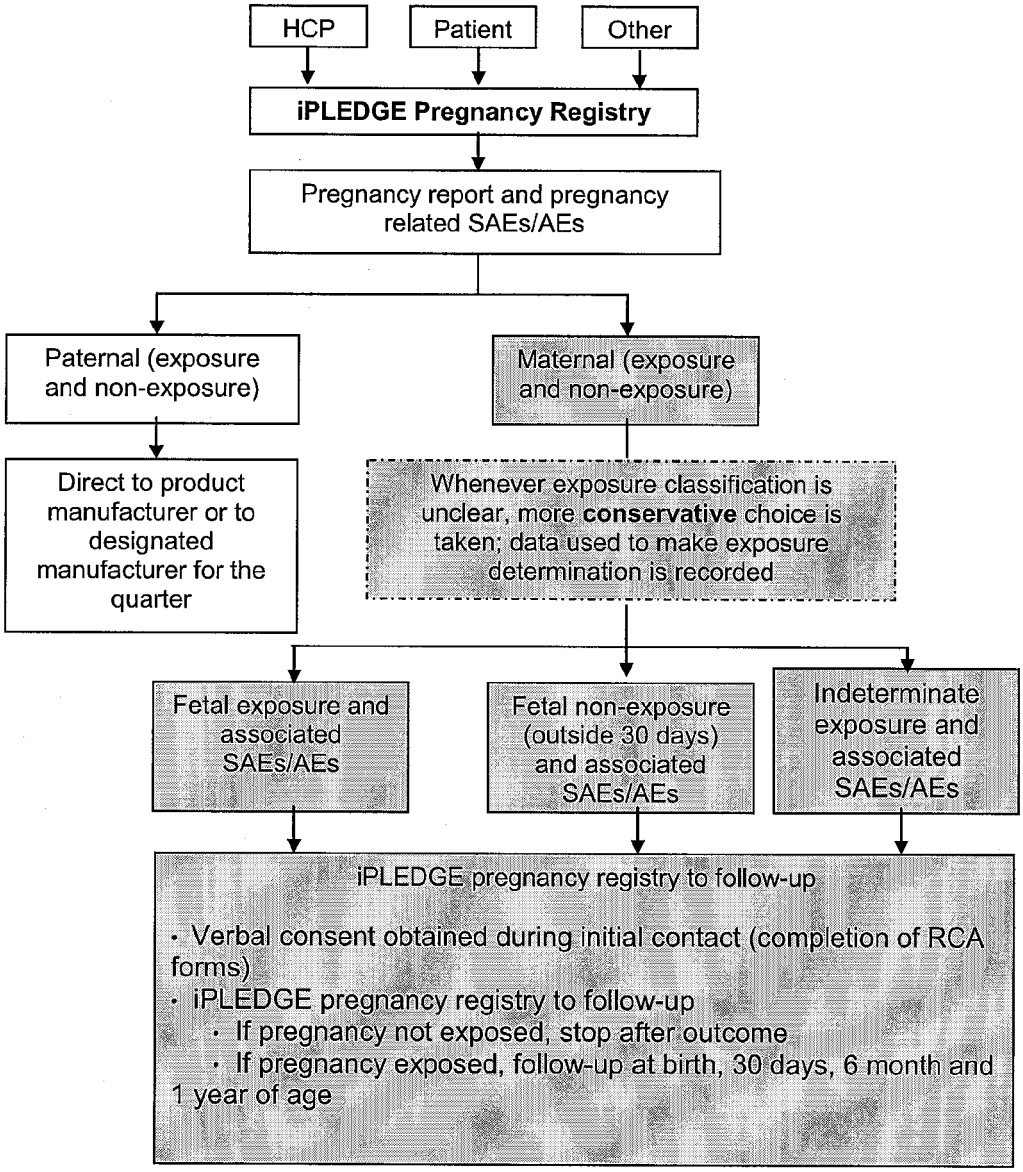
iPLEDGE includes a formal process called lost to follow-up that follows-up with prescribers and female patients of childbearing potential if expected pregnancy test results are not entered into the system. When the system detects that a patient may be lost to follow-up, iPLEDGE representatives will contact the prescriber and provide reminders about posttreatment pregnancy tests to ensure the patient has not become pregnant. Initially, two telephone attempts are made to contact the prescriber. If unsuccessful, a traceable letter is sent to the prescriber within 5 days after the second telephone attempt was made. If all attempts to reach the prescriber are unsuccessful, two telephone attempts are made to contact the patient. If unsuccessful, a traceable letter is sent to the patient, within 5 days after the second telephone attempt was made, which provides the patient with a reminder and requests the patient to contact her prescriber and iPLEDGE.

3.4 Pregnancy Registry

A centralized pregnancy registry for reporting, confirming, and follow-up of all pregnancies was established with the iPLEDGE program. The dataflow for the pregnancy registry is outlined in Figure 3. The objectives of the iPLEDGE pregnancy registry are to: 1) determine the isotretinoin exposure status for each reported pregnancy, 2) document the outcome of each isotretinoin-exposed pregnancy; and 3) provide additional information for each pregnancy to allow for evaluation of the underlying cause(s) (ie, root cause analysis). The root cause analysis questionnaire is provided in Appendix 2.

Data from the registry are reported quarterly to the FDA.

Figure 3 **iPLEDGE Pregnancy Registry Dataflow**



3.5 Postimplementation Program Changes

Shortly after the iPLEDGE program began accepting patient registrations, the sponsors began to receive stakeholder feedback on the operational aspects of the program. Stakeholder feedback was received: 1) through call center interactions, 2) through the iPLEDGE Scientific Advisory Board, 3) through letters to and meetings with the sponsors and FDA from various professional organizations (American Association of Dermatologists, Healthcare Distribution Management Association, National Association of Chain Drug Stores); and 4) through usability testing of the iPLEDGE system.

As a consequence of this feedback, several changes were made to the iPLEDGE program to facilitate the tasks of the various stakeholders (Appendix 3). These changes included allowing the prescriber to reset their iPLEDGE password and the removal of the 23-day lockout period for requalification for a new isotretinoin prescription, if the previous 7-day window for prescription fill was missed by male or female patients of nonchildbearing potential.

Before implementation, all changes were approved by the Agency. Some of the changes were also discussed at a Drug Safety and Risk Management Advisory Committee meeting on February 10, 2006. The Scientific Advisory Board for iPLEDGE was also involved in planning these changes and assisted in communicating these changes to their constituents.

3.6 Proposed iPLEDGE Program Changes

Several other iPLEDGE program changes have been under discussion with the Agency (supplement 58) and are currently under review, with a planned launch date of September 2007. These changes include:

- For females of childbearing potential, changing the start of the 7-day window for a prescription to be filled from the date of the prescriber's office visit to the date of specimen collection for the pregnancy test. This would allow patients to obtain all lab work prior to the prescriber's office visit and for prescribers to have the pregnancy test results at the time of the office visit, thereby mirroring the current office practices of many isotretinoin prescribers.
- Removing the 23-day lockout period after missing the 7-day window for females of childbearing potential to allow them to obtain another prescription as long as all iPLEDGE requirements are satisfied. This change is proposed because prescribers and patients are finding that the 23-day lockout period interferes with office visit scheduling, dose adjustments, vacations, and insurance practices. The exception would be for the **first** isotretinoin prescription where the next CLIA-certified pregnancy test to start the 7-day window over again would have to be at least 19 days after the pregnancy test that started the first 7-day window (the first test is to be tied to the first 5 days of the menstrual cycle).
- Modifying the list of acceptable forms of secondary contraception to allow male latex condoms to be used with or without spermicide. This was a request of the FDA because of concerns that spermicide may affect the structural integrity of condoms thereby increasing the risk of a sexually transmitted disease.

A number of other changes have been proposed to facilitate stakeholder interactions with the iPLEDGE system (Appendix 4). These proposed changes include enhancing system messages to provide greater user assistance, providing links on the iPLEDGE website to the next logical action, adding user navigation and step-by-step data entry, and providing a graphical display of patient status.

4. iPLEDGE EVALUATION

4.1 Wholesalers, Pharmacies, and Prescriber Registration

The total number of wholesalers, pharmacies, and prescribers registered in the iPLEDGE program as of February 28, 2007 is provided in Table 2.

One pharmacy was involuntarily deactivated for dispensing isotretinoin without obtaining authorization for an iPLEDGE patient in the iPLEDGE system. The responsible site pharmacist for this pharmacy stated that he did not want to comply with the iPLEDGE requirements.

Of the registered and activated prescribers, 58% were dermatologists and 23% were family/general practitioners. There were two involuntary prescriber deactivations. One involuntary deactivation was because a negative pregnancy test was entered for a female of childbearing potential without having the pregnancy test result available. The patient self-reported to be pregnant at that time. The other involuntary deactivation occurred when a prescriber gave a patient drug outside of the iPLEDGE program guidelines. This prescriber supplied the patient with Accutane samples during her 30-day waiting period for her first prescription. These samples were in the prescriber's possession and were left over from the Roche Patient Assistance Program (discontinued July 1, 2005).

Table 2 Wholesaler, Pharmacy, and Prescriber iPLEDGE Registrations - iPLEDGE Year One

Type of Registrant	Total Number
Wholesalers	189
Pharmacies	42,362
Prescribers	15,742
Dermatologists	9,132 (58%)
Family/General Practitioners	3, 572 (23%)
Other	3,038 (19%)

4.2 Patient Registration

At the end of the first year, there were 305,366 patients registered in the iPLEDGE program. Most patients were males (50.6%) or females of childbearing potential (45%) (Table 3).

Table 3 Patients Registered in the iPLEDGE Program by Patient Risk Category[1]

Risk Category	N	%
Males	154,515	50.6
Females of childbearing potential	137,415	45
Females not of childbearing potential	13,436	4.4
Total	305,366	

[1]December 30, 2005 to February 28, 2007

4.3 Prescriptions Authorized

During the first year of iPLEDGE, there were 730,732 isotretinoin prescriptions authorized for dispensing with most authorized for males (56.4%) or females of childbearing potential (39.2%) (Table 4).

Of the 137,415 females of childbearing potential registered in iPLEDGE, 91,894 had at least one isotretinoin prescription authorized through the iPLEDGE system. A total of 286,305 isotretinoin prescriptions were authorized during the first year of iPLEDGE for female patients of childbearing potential.

Table 4 Total Number of Isotretinoin Prescriptions Authorized by Patient Risk Category - iPLEDGE Year One

Risk Category	N	%
Males	412,482	56.4
Females of childbearing potential	286,305	39.2
Females not of childbearing potential	31,936	4.4
Total	730,732	

4.4 Prescriptions Denied

During the first year of the iPLEDGE program, there were 135,926 unique patients that had at least one prescription denied (Table 5). Most of these denials were for males (52.1%) or females of childbearing potential (44%). Patients may been denied in the system for multiple reasons, with each reason (eg, counseling not entered, pregnancy test results not entered, etc) being counted in the overall total. Patients may also have been denied because they made multiple attempts to fill the same prescription. Patients who initially had a prescription denied may have subsequently had a prescription authorized if they fulfilled all iPLEDGE requirements.

The most frequent reasons for prescription fill denial for females of childbearing potential were:

- Patient was in the 7-day window and she attempted to fill a prescription without answering her monthly questions.
- Patient was in the 7-day window and she attempted to fill a prescription, but the prescriber had not entered the pregnancy test results.
- Patient missed the 7-day prescription window.

- Prescriber did not confirm patient counseling.
- Only one prescription can be filled per month.

The most frequent reasons for prescription fill denial for males and nonchildbearing females were:

- Patient missed the 7-day prescription window. Since removal of the 23-day lockout period for requalification for a new isotretinoin prescription for males and females of nonchildbearing potential, this is no longer a reason for prescription fill denial (see Section 3.5).
- Prescriber did not confirm patient counseling.
- Only one prescription can be filled per month.

These data demonstrate that pharmacists are adhering to the iPLEDGE requirements before dispensing isotretinoin.

Table 5 Number of Patients With At Least One Isotretinoin Prescription Denied by Patient Risk Category - iPLEDGE Year One

Risk Category	N	%
Males	70,850	52.1
Females of childbearing potential	59,840	44.0
Females NOT of childbearing potential	5236	3.9
Total	135,926	

4.5 Patient Behavior and Program Adherence Assessment

Specific information on patient counseling, use of the patient educational components of iPLEDGE, and contraceptive practices are captured for female patients of childbearing potential in the iPLEDGE system through their monthly input. These data have been summarized to determine patient and prescriber behavior with respect to the iPLEDGE program requirements.

4.5.1 Patient Understanding of the iPLEDGE Program

In order to qualify to receive her first isotretinoin prescription, a female of childbearing potential must also interact with the iPLEDGE system to answer a series of questions to determine if she received the educational material that was to be provided by her prescriber. Note that the numbers reported for these questions are the count of the responses provided at the time she answered her monthly questions about the need to use contraception and the risk of birth defects correctly.

Most female patients of childbearing potential indicated that they were told to avoid pregnancy and that they received an educational kit for female patients who can get pregnant (Section 4.6.2.4 - Table 10). Most also reported reading the *iPLEDGE Program Guide* to *Isotretinoin for Female Patients who Can Get Pregnant* and completing the *iPLEDGE Program Birth Control Workbook* (Section 4.6.2.4 - Table 10).

Slightly more than half of the females of childbearing potential watched the "Be Aware: The Risk of Pregnancy While on Isotretinoin" and "Be Prepared, Be Protected" videos (Section 4.6.2.4 - Table 10).

The majority of patients reported receiving birth control counseling with most receiving counseling by their doctor (Section 4.6.2.4 - Table 11). Thirteen percent of patients reported not receiving any birth control counseling. Approximately half of the patients reported that their prescriber offered to refer them to another healthcare provider for birth control counseling (Section 4.6.2.4 - Table 11).

The majority of females of childbearing potential demonstrated an understanding of the need to use contraception and the risk of birth defects for isotretinoin-exposed pregnancies by passing their monthly comprehension test the first time it was taken (Section 4.6.2.4 - Table 12).

4.5.2 Contraceptive Data

All females of childbearing potential reported compliance with the contraceptive requirements of iPLEDGE (Table 6). The most common contraceptive choices were abstinence and birth control pills and male condoms (Table 6).

Table 6 Contraception Most Frequently Used by Female Patients of Childbearing Potential - iPLEDGE Year One

Primary	Secondary	Percentage
Abstinence	-	43.1
Birth control pills	Male condom	42.0
Vasectomy	Male condom	3.3
Other combinations		11.6

4.6 Pregnancies

Information is provided for all pregnancies where:

- The patient was enrolled in iPLEDGE; and
- The pregnancy report was received by March 31, 2007; and
- Isotretinoin therapy was initiated between December 31, 2005 to March 31, 2007 with the conception date on or before February 28, 2007.

4.6.1 Case Reports

A total of 122 pregnancies were reported to the pregnancy registry and had an isotretinoin prescription authorized through the iPLEDGE program.

4.6.2 Analyses of Pregnancies

Information is provided for the iPLEDGE pregnancies reported during Year One.

4.6.2.1 *Timing of Isotretinoin Exposure Relative to Pregnancy*

The majority of patients became pregnant after isotretinoin therapy was initiated with 10 patients initiating isotretinoin while pregnant and 8 patients becoming pregnant within 30 days after stopping isotretinoin therapy (Table 7).

Table 7 Timing of Exposure of Isotretinoin Therapy Relative to Pregnancy- iPLEDGE Year One

	N (%)
Pregnant when isotretinoin started	10 (8.2)
Taking isotretinoin when pregnancy occurred	78 (63.9)
Became pregnant within 30 days after stopping isotretinoin therapy	8 (6.6)
Unknown	26 (21.3)
Total	122 (100)

4.6.2.2 *Patient Age*

Most of the women who became pregnant were over the age of 20 years (Table 8).

Table 8 Patient Age, Nonpregnant versus Pregnant Females – iPLEDGE Year One

Age Range (years)	Nonpregnant (N=97,886) n (%)	Pregnant (N=122) n (%)
< 12	116 (0.1)	-
12-15	11,579 (11.8)	2 (1.6)
16-19	30,653 (31.3)	24 (19.7)
20-29	34,550 (35.3)	68 (55.7)
30-39	14,846 (15.2)	23 (18.9)
40-44	4, 296 (4.4)	5 (4.1)
≥ 45	1,848 (1.9%)	-

4.6.2.3 *Methods of Contraception*

Oral contraceptives and male condoms were the most frequent primary and secondary methods of contraception for the women who became pregnant (Table 9). Abstinence was the primary method of contraception for 18.3% of the women who became pregnant.

Table 9 Methods of Contraception – Pregnancy Cases (N=112*), iPLEDGE Year One

Primary	Secondary	Percentage
Birth control pills	Male condom	72.2
Abstinence	-	18.3
Hormonal injection	Male condom	3.2
Other combinations		6.3

*10 pregnant patients did not provide their methods of contraception

4.6.2.4 Patient Understanding of the iPLEDGE Program

Almost all of the pregnant women reported that they were told to avoid pregnancy and that they had received an educational kit for female patients who can get pregnant (Table 10). Most of the pregnant women reported reading the *iPLEDGE Program Guide to Isotretinoin for Female Patients Who Can Get Pregnant* and completing the *iPLEDGE Program Birth Control Workbook* (Table 10). This is similar to what the nonpregnant women reported.

More pregnant women than nonpregnant women watched the "Be Aware: The Risks of Pregnancy While on Isotretinoin" and "Be Prepared, Be Protected" videos (Table 10).

The majority of pregnant women reported receiving birth control counseling with most receiving counseling by their doctor (Table 11). Approximately 13% of pregnant women reported not receiving any birth control counseling. This is similar to what was reported by nonpregnant women. A higher percentage of pregnant women compared to nonpregnant women reported that their prescriber offered to refer them to another healthcare provider for birth control counseling (Table 11).

The majority of pregnant women demonstrated an understanding of the need to use contraception and the risk of birth defects for isotretinoin-exposed pregnancies by passing their monthly comprehension test the first time it was taken (Table 12). The percentages of pregnant versus nonpregnant females who failed these tests once or twice before passing was similar.

Table 10 First Month Questions About Avoiding Pregnancy and the Educational Components of iPLEDGE (Patient Self-Reported) – Pregnancy Cases, iPLEDGE Year One[1]

	Percentage of Patients Responding Affirmatively	
	Nonpregnant N=97,151*	Pregnant N=113**
	n (%)	n (%)
Told to avoid pregnancy	96,870 (99.7)	112 (99.1)
Received educational kit for female patients who may get pregnant	95,611 (98.4)	110 (97.3)
Read guide to isotretinoin for female patients who may get pregnant	95,250 (98.0)	109 (96.5)
Read birth control workbook	93,691 (96.4)	108 (95.6)
Watched "Be Aware" video	53,922 (55.5)	77 (68.1)
Watched "Be Prepared, Be Protected" video	53,860 (55.4)	75 (66.4)

*62 nonpregnant patients did not answer the first month questions
**9 pregnant patients did not answer the first month questions
[1]Data for time period between March 1, 2006 to February 28, 2007

Table 11 First Month Questions for Females of Childbearing Potential about Contraceptive Counseling (Patient Self-Reported) - Pregnancy Cases, iPLEDGE Year One[1]

	Percentage of Patients Responding Affirmatively	
	n (%)	n (%)
	Nonpregnant N=97,151*	Pregnant N=113**
Doctor offered to refer for birth control counseling	47,695 (49.1)	62 (54.9)
Contraception counseling provided by		
My doctor	63,870 (65.7))	64 (56.6)
Another healthcare provider	19,991 (20.6)	34 (30.1)
I did not receive counseling	13,289 (13.7)	15 (13.3)

*62 nonpregnant patients did not answer the first month questions
**9 pregnant patients did not answer the first month questions
[1]Data for time period between March 1, 2006 to February 28, 2007

Table 12 Monthly Questions for Females of Childbearing Potential about the Use of Contraception and the Risk of Birth Defects – Pregnancy Cases, iPLEDGE Year One[1]

	Nonpregnant N=97,896 n (%)	Pregnant N=112* n (%)
Passed the first time	81,661 (83.4)	89 (79.4)
1 failure	12,179 (12.4)	21 (18.8)
2 failures	2,681 (2.7)	2 (1.8)
3 failures	780 (0.8)	-
4 failures	294 (0.3)	-
5 failures	122 (0.1)	-
6 failures	57 (< 0.1)	-
7 failures	49 (< 0.1)	-
8 failures	19 (< 0.1)	-
9 failures	14 (< 0.1)	-
10 failures	12 (< 0.1)	-
>10 failures	28 (< 0.1)	-

*10 pregnant patients never took a monthly comprehension test
[1]Data for time period between March 1, 2006 to February 28, 2007

4.6.2.5 Identification of Reasons for Pregnancies

Most of the pregnancies during isotretinoin therapy were due to patient noncompliance with birth control methods (Table 13).

Of the 10 patients who initiated isotretinoin while already pregnant, 3 patients had contraceptive failure, 2 patients were unsuccessful at abstinence, 2 patients did not use two forms of birth control, 2 patients had a prescriber or prescriber designee who falsified the pregnancy test results, and 1 patient had access to isotretinoin from a prescription filled several years earlier.

Of the 8 patients who became pregnant within 30 days of stopping isotretinoin therapy, 2 patients failed to use contraception, 1 patient did not always use two forms of contraception, 1 patient had contraceptive failure, 1 patient was unsuccessful at abstinence, and 1 patient stopped using contraception when isotretinoin therapy was stopped; the reason was unknown by the healthcare provider for 2 of these patients.

Table 13 Reasons for Pregnancies as Reported by the Health Care Provider – Pregnancies During Isotretinoin Therapy (N=87*), iPLEDGE Year One[1]

Reason for pregnancy	Number
Contraceptive failure	23
Failure to use contraceptive on date of conception	14
Did not use two forms of birth control	16
Unsuccessful abstinence	14
Used ineffective contraception	1
Planned pregnancy	0
Unknown	42

*The healthcare provider did not provide any reason for pregnancy in 35 cases.
[1]Categories for reasons for pregnancies are not mutually exclusive so one patient may be in multiple categories

5. OVERALL ASSESSMENT

The main highlights from the iPLEDGE Year One update are as follows:

- The iPLEDGE program is a risk management program of unprecedented size and scope with over 189 wholesalers, 42,362 pharmacies, 15,742 prescribers, and 305,366 patients.
- The majority of the recommended stakeholder changes to increase stakeholder efficiency have been or are in the process of being implemented into the program.
- A centralized isotretinoin pregnancy registry was established and data from its first year provide a baseline for subsequent comparisons.
- Educational messages about the need to avoid pregnancy and to use two forms of contraception for 1 month before, during, and 1 month after isotretinoin therapy are being communicated by prescribers and are reaching female patients of childbearing potential.
- Overall, 137,415 females of childbearing potential were registered during Year One and 91,894 of these patients had an isotretinoin prescription authorized through the iPLEDGE system. A total of 122 pregnancies were reported. The majority of these pregnancies occurred after isotretinoin therapy was initiated. Most pregnancies were associated with contraceptive noncompliance.
- Almost all pregnant and nonpregnant women demonstrated an understanding of both the need to use contraception and the risk of birth defects for isotretinoin-exposed pregnancies.

Appendix 1 Isotretinoin Pregnancy Risk Management Milestones

Date	Action
May 1982	US approval with pregnancy Contraindication.
August 1983	Bold print pregnancy warnings in Contraindications, Warnings, and Precautions sections.
February 1984	Black Box pregnancy warnings added.
August 1988	Avoid pregnancy logo inserted.
October 1988	Pregnancy Prevention Program (PPP) initiated Two forms of contraception Negative monthly pregnancy test "Avoid pregnancy" symbol in packaging Educational materials regarding contraceptives and pregnancy avoidance Female patient informed consent form Evaluation tools for effectiveness of PPP (Accutane Survey).
April 1990	Birth defects information included in Black Box.
April 1990	Recommendation to prescribe only one month supply added
December 1993	Need for pregnancy testing added to Black Box.
January 1994	Updated patient consent form to include additional requirements
May 2000	Two negative pregnancy tests prior to initial prescription Accutane Medication Guide distributed with the Accutane BlisterPak™. Required female patients to view a non-branded videotape on contraception.
September 2000	Drug Safety Risk Management Advisory Committee
October 2001	Pregnancy test of at least 25 mIU β-HCG required.
January 2002	System to Manage Accutane Related Teratogenicity™ initiated. In addition to components of PPP: • Link dispensing to negative pregnancy testing (via Accutane Qualification Sticker) • Enhanced educational components • Enhanced informed consent • Registration of prescribers
November 2002	S.P.I.R.I.T. Risk Management Program (Amnesteem)[1]
December 2002	I.M.P.A.R.T. Risk Management Program (Sotret)[2]
April 2003	A.L.E.R.T. Risk Management Program (Claravis)[3]
February, 2004	Drug Safety Risk Management Advisory Committee to discuss S.M.A.R.T. Year 1 results and a sponsor proposal for an isotretinoin registry
August, 2005	iPLEDGE Approved by FDA
December, 2005	Launch of iPLEDGE
February, 2006	Drug Safety Risk Management Advisory Committee meeting to discuss the operational aspects of iPLEDGE

[1]System to Prevent Isotretinoin-Related Issues and Teratogenicity
[2]Isotretinoin Medication Program Alerting You to the Risks of Teratogenicity
[3]Adverse Event Learning and Education Regarding Teratogenicity

Appendix 2 Root Cause Analysis Questionnaire

1. Patient Information:

Your name: _____

Address:_____ City_____ State____ Zip_____

Your Telephone: ____-____-_____ Your Fax: ____-____-_____

Your Email: _____ Cell Phone: ____-____-_____

The last 4 digits of your Social Security Number: _____

Date of Birth: _____ Your Age at Conception: _____

Are you enrolled in the iPLEDGE program? ___Yes ___No ___Don't know

2. Secondary Contact Information: (family member or friend who will always know how to contact you)

Name: _____

Address:_____ City_____ State____ Zip_____

Telephone: ____-____-_____ Fax: ____-____-_____

Email: _____ Cell Phone: ____-____-_____

3. Race/Ethnicity Information:

What is your race?

___Caucasian ___Asian

___Black/African American ___Other, specify_____

___Native American ___Don't Know/Prefer not to answer

Are you Hispanic? ___Yes ___No

4. Language Information:

Are you comfortable speaking English? ___Yes ___No

What is your native language?

___English ___Other, specify_____

___Spanish ___Don't Know/Prefer not to answer

5. Pregnancy Information:

What was the first day of your last menstrual period? _____

What was the approximate date you became pregnant? _____

What date was your pregnancy test positive? _____

When is your approximate due date? _____

6. What was the date that the positive pregnancy test was taken?

☐☐/☐☐/☐☐☐☐

Month Day Year

What was the type of pregnancy test?

Laboratory:

☐Blood Test Serum hCG result if known: _____ ☐Urine

Non Laboratory:

☐At-home urine pregnancy test ☐Office urine pregnancy test

Other:

☐ Type Unknown ☐ Not done

7. Isotretinoin Information:

Which isotretinoin product did you use? (Product 1):

Manufacturer: Accutane® Roche ☐ Claravis® Barr ☐

Amnesteem® Mylan ☐ Sotret® Ranbaxy ☐ Unknown ☐

Have you taken isotretinoin during your pregnancy?

___Yes ___No ___Don't know

When did you begin taking isotretinoin?

___before I became pregnant

___after I became pregnant

What was the approximate date you started taking isotretinoin?

_____

What was the approximate last day you took isotretinoin? _____

Capsule Strength: _____ How often did you take isotretinoin? _____

_____

Lot#: _____ Expiration Date: ☐☐/☐☐/☐☐☐☐

Month Day Year

Which isotretinoin product did you use? (Product 2):

Manufacturer: Accutane® Roche ☐ Claravis® Barr ☐

Amnesteem® Mylan ☐ Sotret® Ranbaxy ☐ Unknown ☐

Have you taken isotretinoin during your pregnancy?

___Yes ___No ___Don't know

When did you begin taking isotretinoin?

___before I became pregnant

___after I became pregnant

What was the approximate date you started taking isotretinoin?

_____

What was the approximate last day you took isotretinoin? _____

Capsule Strength: _____ How often did you take isotretinoin? _____

_____

Lot#: _____ Expiration Date: ☐☐/☐☐/☐☐☐☐

Month Day Year

_____

8. Isotretinoin Prescriber Information:

Was isotretinoin prescribed for you by a doctor? ___Yes ___No
(if no, go to question 9)

Who prescribed isotretinoin for you?

___Dermatologist ___Family Doctor

___Oncologist (cancer doctor) ___Other, specify_____

___Pediatrician ___Isotretinoin was not prescribed for me
(if checked, go to question 9)

Prescriber's Name: _____

Address:_____ City_____ State____ Zip_____

Telephone: ____-____-_____ Fax: ____-____-_____

Is your prescriber aware of your pregnancy? ___Yes ___No ___Don't know

9. Where did you obtain isotretinoin?

___Pharmacy (if checked go to question 10)

___Friend/Relative (if checked go to question 11)

___Internet (if checked go to question 12)

___Other, please specify_____
_____

10. Pharmacy Information:

Name: _____

Address:_____ City_____ State____ Zip_____

Telephone: ____-____-_____ Fax: ____-____-_____

11. If you obtained isotretinoin from a friend or relative was this person…

___male

___female

___prefer not to answer

___not applicable

Was the friend or relative participating in the iPLEDGE program? ___Yes ___No ___Don't know

Why did you obtain isotretinoin from the friend or relative? *(check all that apply)*

___I heard it was hard to get

___I didn't want to see a doctor

___I didn't want my parents to know

___Other, please specify_____
_____

12. Why did you obtain isotretinoin from the internet *(check all that apply)*

___I heard it was hard to get

___I didn't want to see a doctor

___I didn't want my parents to know

___Other, please specify_____
_____
_____

13. In the ***30 days before starting isotretinoin*** did any of the following apply? *(check all that apply)*

Not sexually active, not using birth control	___Yes	___No	___Don't know/Don't remember
Not sexually active, using birth control	___Yes	___No	___Don't know/Don't remember
Sexually active, using birth control	___Yes	___No	___Don't know/Don't remember
Sexually active, not using birth control	___Yes	___No	___Don't know/Don't remember
Told or thought I was post menopausal	___Yes	___No	___Don't know/Don't remember

14. In the ***30 days before starting isotretinoin*** were you using any of the following methods of birth control? *(check all that apply)*

_____Not using birth control

___Abstinence

___Cervical Cap

___Cervical Shield

___ Combination Oral Contraceptive (birth control pills)

___Condom (Male)

___Condom (Female)

___Depo Provera (Injectable Hormones)

___Diaphragm

___Female Sterilization (tubes tied)

___Hormonal Patch

___Hormonal Vaginal Contraceptive Ring (Nuva Ring)

___Intrauterine device (IUD) LNg20 (Mirena or ParaGard T380A

___Intrauterine Device (IUD) (Progesterone T)

___Implantable Hormones (Norplant)

___Male Sterilization (partner's vasectomy)

___Mini Pills (Progestin only such as Ortho Micronor or Ovrette)

___Morning-after pill/emergency contraception

___Natural Family Planning (rhythm method)

___Vaginal Contraceptive Suppository

___Vaginal Sponge

___Withdrawal

Other, Specify_____-

15. In the ***30 days before starting isotretinoin*** did you use 2 forms of birth control together every time you had sex?

___Yes ___No ___Don't know/Don't remember

16. In the ***month before you became pregnant*** did any of the following apply? *(check all that apply)*

Not sexually active, not using birth control	___Yes	___No	___Don't know/Don't remember
Not sexually active, using birth control	___Yes	___No	___Don't know/Don't remember
Sexually active, using birth control	___Yes	___No	___Don't know/Don't remember
Sexually active, not using birth control	___Yes	___No	___Don't know/Don't remember
Told or thought I was post menopausal	___Yes	___No	___Don't know/Don't remember

17. In the ***month before you became pregnant*** were you using any of the following methods of birth control? *(check all that apply)*

_____Not using birth control	___Intrauterine device (IUD) LNg20 (Mirena or ParaGard T380A
___Abstinence	___Intrauterine Device (IUD) (Progesterone T)
___Cervical Cap	___Implantable Hormones (Norplant)
___Cervical Shield	___Male Sterilization (partner's vasectomy)
___ Combination Oral Contraceptive (birth control pills)	___Mini Pills (Progestin only such as Ortho Micronor or Ovrette)
___Condom (Male)	___Morning-after pill/emergency contraception
___Condom (Female)	
___Depo Provera (Injectable Hormones)	___Natural Family Planning (rhythm method)
___Diaphragm	___Vaginal Contraceptive Suppository
___Female Sterilization (tubes tied)	___Vaginal Sponge
___Hormonal Patch	___Withdrawal
___Hormonal Vaginal Contraceptive Ring (Nuva Ring)	Other, Specify_____

18. In the ***month before you became pregnant*** did you use 2 forms of birth control together every time you had sex?

___Yes ___No ___Don't know/Don't remember

19. *When you became pregnant* were you using any of the following methods of birth control? *(check all that apply)*

___Not using birth control

___Abstinence

___Cervical Cap

___Cervical Shield

___ Combination Oral Contraceptive (birth control pills)

___Condom (Male)

___Condom (Female)

___Depo Provera (Injectable Hormones)

___Diaphragm

___Female Sterilization (tubes tied)

___Hormonal Patch

___Hormonal Vaginal Contraceptive Ring (Nuva Ring)

___Intrauterine device IUD LNg20 (Mirena or ParaGard T380A

___Intrauterine Device (IUD) (Progesterone T)

___Implantable Hormones (Norplant)

___Male Sterilization (partner's vasectomy)

___Mini Pills (Progestin only such as Ortho Micronor or Orvette)

___Morning-after pill/emergency contraception

___Natural Family Planning (rhythm method)

___Vaginal Contraceptive Suppository

___Vaginal Sponge

___Withdrawal

Other, Specify

20. How often have you had sexual intercourse during treatment with isotretinoin ***without using any*** birth control?

___Always (did not use birth control at any time during isotretinoin therapy)

___Usually (more than half of the time)

___Sometimes (Less than half of the time)

___Never (always use birth control)

21. How often have you had sexual intercourse during treatment with isotretinoin ***using only one*** form of birth control?

___Always (never used more than one form of birth control)

___Usually (more than half of the time)

___Sometimes (Less than half of the time)

___Never (always used 2 forms of birth control)

22. If you used emergency birth control ("Morning After" pill or emergency IUD) during isotretinoin treatment, how often did this occur?

___Once

___Twice

___Three times or more

___Never

23. Please check the boxes that best describe what you think contributed to your becoming pregnant.
(check all that apply)

___Birth control failed

___Missed pills

___Did not use birth control the day I got pregnant

___Did not use 2 forms of birth control

___Partner did not use condom

___Condom broke/slipped off

___Hormone patch fell off

___Vaginal Ring fell out

___Did not get hormone injection

___Did not use spermicide with condom, cervical cap, or diaphragm

___Unsuccessful at abstinence

___Unplanned sex

___Alcohol use

___Other, specify_____

___Unknown

Please explain:_____
_____
_____

24. ***When you became pregnant*** did you use 2 forms of birth control together?

___Yes ___No ___Don't know/Don't remember

25. Do you recall if you were drinking alcohol when you got pregnant?

___Yes ___No ___Don't know/Don't remember

26. If you missed taking birth control pills in the month before you became pregnant, how often did this occur?

___One time

___Two times

___Three times or more

___Never

___NA (not taking birth control pills)

What was the greatest number of days that you missed?

___One day

___Two days

___Three days or more

___Never

___Don't know/Don't remember

27. If your hormone patch fell off in the month before you became pregnant, how often did this occur?

___One time

___Two times

___Three times or more

___Never

___NA (not using hormone patch)

What was the greatest number of days that your patch was off?

___One day

___Two days

___Three days or more

___Never

___Don't know/Don't remember

28. If your Vaginal Ring slipped out in the month before you became pregnant, how often did this occur?

___One time
___Two times
___Three times or more
___Never
___NA (not using vaginal ring)

What was the greatest number of days that your ring was out?

___One day
___Two days
___Three days or more
___Never
___Don't know/don't remember

29. If you reported using **Depo Provera® during** isotretinoin treatment, how often were any injections given more than 13 weeks apart?

___Once
___Twice
___Three or more times
___Never
___Don't know/Don't remember
___NA (Not receiving injections)

30. What is the highest level of education that you completed?

___Grades 0-8
___Grades 9-11
___High School Graduate
___Some College
___College Graduate
___Post Graduate Degree
___Don't know/Prefer not to answer

31. Were you counseled about the risk of birth defects with isotretinoin?

___Yes ___No ___Don't know/Don't remember

32. Were you instructed on how **not** to become pregnant while taking isotretinoin?

___Yes ___No ___Don't know/Don't remember

If yes, by whom: *(check all that apply)*

___Doctor who prescribed isotretinoin

___Gynecologist

___Referred to contraceptive counselor

___Other healthcare provider, Please specify_____

___Other (such as parent, teacher, friend) Please specify_____

33. If you were referred to a contraceptive counselor, was the counseling helpful?

___Very helpful

___Somewhat helpful

___Of little use

___Not helpful

What would make counseling better? _____

_____

34. Were you given an **iPLEDGE Program Guide for Female Patients Who Can Get Pregnant**?

___Yes ___No ___Don't know/Don't remember

If yes, did you read it?

___Yes ___No ___Don't know/Don't remember

If yes, did you understand the information in the guide?

___Yes ___No ___Don't know/Don't remember

35. Were you given an **iPLEDGE Program Birth Control Workbook**?

___Yes ___No ___Don't know/Don't remember

If yes, did you read it?

___Yes ___No ___Don't know/Don't remember

If yes, did you understand the information in the workbook?

___Yes ___No ___Don't know/Don't remember

36. Did you watch the DVD **"Be Prepared, Be Protected; Be Aware: The Risks of Pregnancy** While on Isotretinoin" about effects of isotretinoin?

___Yes ___No ___Don't know/Don't remember

If yes, did you understand the information in the DVD?

___Yes ___No ___Don't know/Don't remember

37. Which of the educational materials was most helpful?

___ iPLEDGE Program Guide for Females Who Can Get Pregnant

___iPLEDGE Program Birth Control Workbook

___DVD ("Be Prepared, Be Protected; Be Aware: The Risks of Pregnancy While on Isotretinoin")

Do you have any other comments, including comments about changes you would make in the educational materials? _____

_____

38. How often do you have a drink containing alcohol?

___Never ___Once a month or less ___Two to four times a month

___ Two to three times a week ___Four or more times a week

On Average how many drinks do you have on a typical day?

___1-2 ___3-4 ___5-6 ___7-9 ___10 or more

39. Are you still pregnant?

___Yes ___No ___Don't know

40. If you answered no to the question above, how did your pregnancy end?

___Delivered baby

___Miscarriage

___Abortion Date: ☐☐/☐☐/☐☐☐☐

Month Day Year

___Prefer not to answer

41. Your Obstetrician's Information: Name: _____ Address:_____ City _____ State_____ Zip _____ Telephone: _____-_____-_____ Fax: _____-_____-_____ Email: _____
Comment: (please provide description of relevant events, lab test results or other findings)

_____

Date: _____

Signature of Individual Completing this Form

Thank you for your time in completing this form.

Appendix 3 Postimplementation Changes to the iPLEDGE Program

Feedback/Suggestion	Change to iPLEDGE Program	Date of Change
Ease of password	Users can now request that passwords be e-mailed to them if they forget them.	April 2006
Start new 7-day window immediately after previous 7-day window for male patients and females of nonchildbearing potential	Changed the 23 day wait period after missing the 7 day window to allow males and females of nonchildbearing potential to start the process over immediately.	October 2006
Allow entry of 10 and 11 digit National Drug Code numbers	Allowed the use of 10 or 11 digit NDC numbers for pharmacies to fill prescriptions.	January 2007
Extend one-time password usage	One-time password usage was extended to avoid password expiration upon closing the browser, and notices were added to change password prior to closing browser.	January 2007
Allow prescribers and patients to make changes to patient address and date of birth	Allowed prescribers to change patient address, date of birth, and other demographic information in iPLEDGE.	January 2007
Self-print capability for stakeholder materials	Added all materials (consent forms, educational materials, etc) in PDF format to the web site to allow stakeholders to print materials as needed.	January 2007
Update 7-day window expiration verbiage	Updated verbiage on the 7-day window calculation for the pharmacy to clarify what "midnight" on mm/dd/yy actually refers to.	January 2007
Interactive voice recognition log-in	Replaced alphanumeric user IDs; transitioned all numeric user IDs and remove asterisks in data entry for interactive voice recognition log-in	January 2007

Appendix 4 Proposed Changes to the iPLEDGE Program

Feedback/Suggestion	Planned Change to iPLEDGE Program
Replace "acne" attestation with "isotretinoin indication" attestation	Modify prescriber attestation statement from "knowing how to diagnose acne" to "knowing the indication for isotretinoin" to allow oncologists and other prescribers to complete an accurate attestation statement.
Start 7-day window at time of pregnancy test	Change the 7-day window for females of childbearing potential from date of office visit to date of pregnancy test.
Start new 7-day window immediately after previous 7-day window	Change the 23-day waiting period after missing the 7- day window to allow all patients to start the process over immediately. The exception is for females of childbearing potential who missed the 7-day window in their first month of therapy.
Enhance display of patient data, including key dates, 7-day window status, etc.	System to display upcoming key dates as well as other information regarding current status of a patient in the program (7-window expiration etc).
Remove HIPAA checkbox	Remove HIPAA check box from patient registration.
Registration navigation for males and females of nonchildbearing potential	Completion of registration for male patients or females of nonchildbearing potential should take a user directly to the confirmation screen.
Remove contraception bullet point for females of nonchildbearing potential	Remove first bullet point on Confirm Patient Counseling screen for females of nonchildbearing potential, which relates to the requirement to use two forms of contraception.
Enhance system messages for user assistance	Add more helpful error messages, eg, replace "See your doctor" or "Patient requires confirmation" and other similar messages to generally provide more information regarding the cause of certain status values and status changes as they occur.
No secondary form required when abstinence is chosen as primary (default to none)	The contraception drop down menu for secondary form should default to "None" if abstinence is selected as the primary form.
Provide "password to be mailed to patient" message to prescriber upon registration completion	At the end of registration, tell the prescriber that the patient's password will be mailed to him or her.

EXHIBIT 4

Celgene Licenses S.T.E.P.S.(R) Use Patents to Isotretinoin Manufacturers for Safe Distribution of Isotretinoin for Treatment of Severe Recalcitrant Nodular Acne

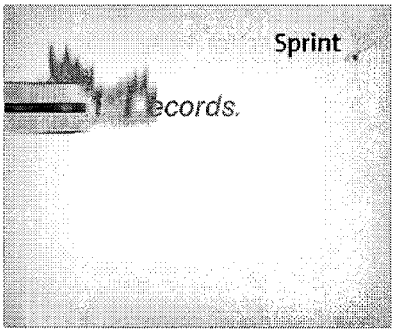
Posted on: Tuesday, 23 November 2004, 12:00 CST

WARREN, N.J., Nov. 23 /PRNewswire-FirstCall/ -- Celgene Corporation announced an agreement providing Barr Pharmaceuticals, Inc. , Mylan/Bertek on behalf of Genpharm, Ranbaxy, and Roche with a non- exclusive license to its patent portfolio directed to methods of safely delivering drugs in potentially high risk patient populations. The manufacturers of isotretinoin have licensed these patents with the intention of implementing a new pregnancy risk management system for isotretinoin. The patents are directed to, among other things, Celgene's proprietary S.T.E.P.S. (System for Thalidomide Education and Prescribing Safety) program. S.T.E.P.S. is the first FDA-approved managed closed-loop pharmaceutical delivery and restrictive distribution program, and it is protected by a network of multiple patents, including use patents, with long remaining terms. Nearly 115,000 patients have taken advantage of this pharmaceutical delivery program since its inception in the summer of 1998. S.T.E.P.S. involves patients, prescribers and pharmacists, and it can serve as a successful blueprint for the appropriate distribution of any pharmaceutical that offers important therapeutic benefits but has serious side effects.

"We are very proud of our approach to risk management, as exemplified by our S.T.E.P.S. program and the high standard of controlled pharmaceutical delivery it offers our global industry," said Sol J. Barer, Ph.D., President and Chief Operating Officer of Celgene Corporation. "At Celgene, there is no higher priority than safe access to drugs that enable health care providers to offer significant clinical benefits to patients in need while reducing the risk of serious side-effects."

Abcut S.T.E.P.S.

Celgene developed S.T.E.P.S.(R) (System for Thalidomide Education and Prescribing Safety), the first program in this proprietary type of managed drug distribution, to support the distribution of THALOMID(R) (thalidomide). THALOMID, approved for the acute treatment of cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL) and as maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL recurrence, potentially causes severe birth defects or death to an unborn baby. THALOMID is not indicated as monotherapy for ENL treatment in the presence of moderate to severe neuritis.



S.T.E.P.S., the first FDA-approved managed distribution program, serves as a blueprint for the appropriate distribution of pharmaceutical products that offer important therapeutic benefits but have serious side effects. Celgene has effectively implemented S.T.E.P.S. since the launch of THALOMID in 1998 and during the past six years 115,000 patients, 15,000 prescribers and 23,000 pharmacies have been successfully registered in S.T.E.P.S. to fill close to 700,000 prescriptions for THALOMID. S.T.E.P.S. incorporates state-of-the-art technology to ensure that THALOMID is appropriately distributed and to improve patient care, permit real-time interventions and maximize compliance. For more information on S.T.E.P.S., please visit the Celgene website at http://www.celgene.com/.

Safety Notice

If thalidomide is taken during pregnancy, it can cause severe birth defects or death to an unborn baby. Thalidomide should never be used by women who are pregnant or who could become pregnant while taking the drug. Even a single dose, one capsule (50 mg, 100 mg and 200 mg), taken by a pregnant woman can cause severe birth defects. Because thalidomide is present in the semen of male patients, males receiving thalidomide must always use a latex condom during sexual contact with women of childbearing potential even if he has undergone a successful vasectomy. Thalidomide can only be marketed under a special restricted distribution program. This program is called the "System for Thalidomide Education and Prescribing Safety (S.T.E.P.S.(R)). Under this program, only registered prescribers and pharmacists may dispense the drug. In addition, patients must be advised of, agree to and comply with the requirements of S.T.E.P.S.

Thalidomide is known to cause nerve damage that may be permanent. Peripheral neuropathy is a common, potentially severe, side effect of treatment with thalidomide that may be irreversible. Patients with neoplastic and various inflammatory conditions being treated with thalidomide in combination with other agents may have an increased incidence of thromboembolic events such as pulmonary embolism, deep vein thrombophlebitis, thrombophlebitis, or thrombosis. Decreased white blood cell counts, including neutropenia, have been reported in the clinical use of thalidomide. In placebo controlled clinical trials of HIV-seropositive patient populations, there have been reports of increased plasma HIV RNA levels associated with thalidomide therapy. The most common adverse events observed in clinical use in ENL and HIV-seropositive patient populations are rash, maculo-papular rash, drowsiness/somnolence, peripheral neuropathy, dizziness/orthostatic hypotension, neutropenia, and increased HIV-viral load. Patients should be advised about these associated adverse events and routinely monitored by a physician during treatment with thalidomide. Patients should be instructed to not extensively handle or open thalidomide capsules and to maintain storage of capsules in blister packs until ingestion.

About THALOMID

THALOMID (thalidomide), manufactured by Celgene Corporation, received U.S. Food and Drug Administration (FDA) clearance on July 16, 1998 for the acute treatment of cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL) and as maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL recurrence. Thalidomide is not indicated as monotherapy for ENL treatment in the presence of moderate to severe neuritis. Thalidomide currently has a pending regulatory application (NDA) under review by the Food and Drug Administration (FDA) to confirm efficacy and safety for use in multiple myeloma,

thalidomide is not presently indicated or approved by the FDA for use in the disease or any other related cancer.

About Celgene

Celgene Corporation, headquartered in Warren, New Jersey, is an integrated biopharmaceutical company engaged primarily in the discovery, development and commercialization of novel therapies for the treatment of cancer and inflammatory diseases through gene and protein regulation. For more information, please visit the Company's website at http://www.celgene.com/.

This release contains certain forward-looking statements which involve known and unknown risks, delays, uncertainties and other factors not under the Company's control, which may cause actual results, performance or achievements of the Company to be materially different from the results, performance or other expectations implied by these forward-looking statements. These factors include results of current or pending research and development activities, actions by the FDA and other regulatory authorities, and those factors detailed in the Company's filings with the Securities and Exchange Commission such as 10K, 10Q and 8K reports.

Celgene Corporation

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Application Number:	11437551
Filing Date:	19-May-2006
Title of Invention:	Methods for delivering a drug to a patient while restricting access to the drug by patients for whom the drug may be contraindicated
First Named Inventor/Applicant Name:	Bruce A. Williams
Filer:	Angela Verrecchio/Kelly Freels
Attorney Docket Number:	CELG-0508

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Extension - 2 months with $0 paid	1252	1	490	490

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
			Total in USD ($)	**490**

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EFS ID:	6838258
Application Number:	11437551
International Application Number:	
Confirmation Number:	3533
Title of Invention:	Methods for delivering a drug to a patient while restricting access to the drug by patients for whom the drug may be contraindicated
First Named Inventor/Applicant Name:	Bruce A. Williams
Customer Number:	23377
Filer:	Angela Verrecchio/Kelly Freels
Filer Authorized By:	Angela Verrecchio
Attorney Docket Number:	CELG-0508
Receipt Date:	19-JAN-2010
Filing Date:	19-MAY-2006
Time Stamp:	16:58:36
Application Type:	Utility under 35 USC 111(a)

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Payment Type	Deposit Account
Payment was successfully received in RAM	$490
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Warnings:					
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2	Extension of Time	1466612_1.PDF	322594 7c3ae67c6bc3473603a5e9bd3f5c7d6058366c49	no	2
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3		1466772_1.PDF	3700669 4eefaf7e79e4e319a752d2b6c0de855c36ce4241	yes	79

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	Claims	2	9
	Applicant Arguments/Remarks Made in an Amendment	10	79

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If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/21 (07-09)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission	83

Application Number	11/437,551
Filing Date	May 19, 2006
First Named Inventor	Bruce A. Williams
Art Unit	3769
Examiner Name	Michael C. Astorino
Attorney Docket Number	CELG-0508

ENCLOSURES (*Check all that apply*)

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☑ Amendment/Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☑ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Reply to Missing Parts/ Incomplete Application
  - ☐ Reply to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s) _____
  - ☐ Landscape Table on CD
- ☐ After Allowance Communication to TC
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- ☐ Proprietary Information
- ☐ Status Letter
- ☑ Other Enclosure(s) (please Identify below):

Remarks

Exhibits 1 through 4 attached to Response.

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Woodcock Washburn LLP		
Signature	/Angela Verrecchio/		
Printed name	Angela Verrecchio		
Date	January 19, 2010	Reg. No.	54,510

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

Signature			
Typed or printed name		Date	

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

PTO/SB/22 (07-09)
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PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a) **FY 2009** (*Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).*)	Docket Number (Optional) CELG-0508
Application Number 11/437,551	Filed May 19, 2006
For Methods For Delivering A Drug To A Patient While Restricting Access To The Drug By Patients For Whor	
Art Unit 3769	Examiner Michael C. Astorino

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

		Fee	Small Entity Fee	
☐	One month (37 CFR 1.17(a)(1))	$130	$65	$
☑	Two months (37 CFR 1.17(a)(2))	$490	$245	$ 490.00
☐	Three months (37 CFR 1.17(a)(3))	$1110	$555	$
☐	Four months (37 CFR 1.17(a)(4))	$1730	$865	$
☐	Five months (37 CFR 1.17(a)(5))	$2350	$1175	$

☐ Applicant claims small entity status. See 37 CFR 1.27.

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☑ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 223050.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest. See 37 CFR 3.71.
Statement under 37 CFR 3.73(b) is enclosed (Form PTO/SB/96).

☑ attorney or agent of record. Registration Number 54,510

☐ attorney or agent under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

/Angela Verrecchio/ — Signature

January 19, 2010 — Date

Angela Verrecchio — Typed or printed name

(215) 568-3100 — Telephone Number

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below.

☑ Total of 1 forms are submitted.

This collection of information is required by 37 CFR 1.136(a). The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 6 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number	Filing Date	☐ To be Mailed
11/437,551	05/19/2006	

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE ($)	SMALL ENTITY FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							
			TOTAL			TOTAL	

* If the difference in column 1 is less than zero, enter "0" in column 2.

APPLICATION AS AMENDED – PART II

AMENDMENT	02/25/2010	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	SMALL ENTITY ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 23	Minus	** 24	= 0	X $ =		OR	X $52=	0
	Independent (37 CFR 1.16(h))	* 5	Minus	***5	= 0	X $ =		OR	X $220=	0
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	0

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	SMALL ENTITY ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =		OR	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =		OR	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

Legal Instrument Examiner:
/JAMES w. TUNSTALL/

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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DOCKET NO.: CELG-0508 **PATENT**
Application No.: 11/437,551
Office Action Dated: September 9, 2009

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Bruce A. Williams and Joseph K. Kaminski

Confirmation No.: **3533**

Application No.: **11/437,551**

Group Art Unit: **3769**

Filing Date: **May 19, 2006**

Examiner: **Michael C. Astorino**

For: **Methods For Delivering A Drug To A Patient While Restricting Access To The Drug By Patients For Whom The Drug May Be Contraindicated**

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

SUPPLEMENTAL REPLY PURSUANT TO 37 CFR § 1.111

Supplemental to the Reply filed **January 19, 2010** and in response to the Official Action dated **September 9, 2009**, reconsideration is respectfully requested in view of the amendments and/or remarks as indicated below:

☐ **Amendments to the Specification** begin on page of this paper.

☒ **Amendments to the Claims** are reflected in the listing of the claims which begins on page 2 of this paper.

☐ **Amendments to the Drawings** begin on page of this paper and include an attached replacement sheet.

☒ **Remarks** begin on page 5 of this paper.

☐ **Request For Refund** submitted herewith.

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claims 1-31 (Canceled).

32. (Currently Amended) A method of treating a male patient, suffering from erythema nodosum leprosum, with thalidomide, permitting prescriptions for thalidomide to be filled by a pharmacy only after the pharmacy has retrieved an approval code for the prescription, wherein the generation of the prescription approval code comprises the following steps:

(a) via a computer readable storage medium~~computer~~, registering a prescriber and the pharmacy with a distributor of thalidomide;

(b) determining whether the patient is able to understand and ~~reliably~~ carry out instructions;

(c) upon determination that the patient is able to carry out the instructions, providing verbal ~~oral~~ and written warnings of the hazard of taking thalidomide and exposing fetus to the drug;

(d) further providing verbal ~~oral~~ and written warnings of the risk of possible contraception failure and of the need to use barrier contraception when having sexual intercourse with women of child bearing potential;

(e) obtaining acknowledgement of said warnings from the patient;

(f) via a computer readable storage medium, registering the patient with the distributor; and

(g) upon obtaining the acknowledgement and registrations, generating via a computer readable storage medium~~computer~~ the prescription approval code to be retrieved by the pharmacy before the prescription is filled; and

(h) upon retrieving a prescription approval code, administering thalidomide to the patient.

33. (Previously Presented) The method of claim 32, wherein the acknowledgement requires the patient's acknowledgement of one or more of the following:

(a) the understanding that thalidomide must not be taken if unprotected sex cannot be avoided;

(b) the understanding of potential birth defects;

(c) that the patient has been advised of the need for barrier contraception by the prescriber;

(d) the obligation to inform the prescriber if the patient's sexual partner is suspected of becoming or being pregnant;

(e) that thalidomide is solely for the use of the patient himself and must not be shared with any other person;

(f) that the patient has read the information brochure or viewed the information film on thalidomide;

(g) that the semen or blood must not be donated during the thalidomide treatment;

(h) that all of the patient's inquiries regarding thalidomide treatment have been answered by the prescribing physician; or

(i) the patient's understanding that participation in a survey and patient registry is required during the thalidomide treatment.

34. (Previously Presented) The method of claim 32 further comprising providing the patient, prior to generation of the approval code, with warnings of the side effects associated with administration of thalidomide, wherein said side effects are non-teratogenic side effects.

35. (Previously Presented) The method of claim 32 further comprising obtaining a written authorization by the prescriber prior to generation of the approval code.

36. (Previously Presented) The method of claim 32, wherein the prescription approval code is retrieved from a computer readable storage medium.

37. (Previously Presented) The method of claim 32, wherein the acknowledgement is a written informed consent.

38. (Previously Presented) The method of claim 37, wherein the written informed consent is registered in the medium prior to generation of the prescription approval code.

DOCKET NO.: CELG-0508 **PATENT**
Application No.: 11/437,551
Office Action Dated: September 9, 2009

Claims 39-54 (Canceled)

REMARKS

This Reply is Supplemental to the Reply filed January 19, 2010 in response to the Action dated September 9, 2009. After entry of this amendment, claims 32-38 will be pending.

Claim 32 has been amended. Support for the amendment can be found throughout the specification and claims. Claims 39-54 have been canceled.

The Applicants assert that the pending claims are in condition for allowance. An early Notice to that effect is, therefore, earnestly solicited.

Date: May 6, 2010

/Stephanie A. Barbosa/
Stephanie A. Barbosa
Registration No. 51,430

Woodcock Washburn LLP
Cira Centre
2929 Arch Street, 12th Floor
Philadelphia, PA 19104-2891
Telephone: (215) 568-3100
Facsimile: (215) 568-3439

Electronic Acknowledgement Receipt

EFS ID:	7565971
Application Number:	11437551
International Application Number:	
Confirmation Number:	3533
Title of Invention:	Methods for delivering a drug to a patient while restricting access to the drug by patients for whom the drug may be contraindicated
First Named Inventor/Applicant Name:	Bruce A. Williams
Customer Number:	23377
Filer:	Stephanie A. Barbosa/D. McCarty
Filer Authorized By:	Stephanie A. Barbosa
Attorney Docket Number:	CELG-0508
Receipt Date:	06-MAY-2010
Filing Date:	19-MAY-2006
Time Stamp:	16:43:57
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	CELG-0508TransmittalSupReply.PDF	283092 22230e1c82264ee93944da14ea95edbff12e4568	no	2

Warnings:	
Information:	

2		CELG-0508SupReply.PDF	77117 5296c53eb3c68d52a0a8d85b855c31ffa2606419	yes	5

Multipart Description/PDF files in .zip description

Document Description	Start	End
Supplemental Response or Supplemental Amendment	1	1
Claims	2	4
Applicant Arguments/Remarks Made in an Amendment	5	5

Warnings:

Information:

Total Files Size (in bytes):	360209

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission

Application Number	11/437,551
Filing Date	May 19, 2006
First Named Inventor	Bruce A. Williams
Art Unit	3769
Examiner Name	Michael C. Astorino
Attorney Docket Number	CELG-0508

ENCLOSURES (*Check all that apply*)

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- ☐ Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- ☐ Proprietary Information
- ☐ Status Letter
- ☐ Other Enclosure(s) (please Identify below):

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Woodcock Washburn, LLP		
Signature	/Stephanie A. Barbosa/		
Printed name	Stephanie A. Barbosa		
Date	May 6, 2010	Reg. No.	51,430

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Signature			
Typed or printed name		Date	

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The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/437,551	05/19/2006	Bruce A. Williams	CELG-0508	3533

23377 7590 05/18/2010

WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

EXAMINER	
ASTORINO, MICHAEL C	
ART UNIT	**PAPER NUMBER**
3769	
MAIL DATE	**DELIVERY MODE**
05/18/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Interview Summary	Application No.	Applicant(s)	
	11/437,551	WILLIAMS ET AL.	
	Examiner	Art Unit	
	Michael C. Astorino	3769	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Michael C. Astorino*. (3)_____.

(2) *Stephanie Barbosa*. (4)_____.

Date of Interview: *4/21-5/06, 2010*.

Type: a)☒ Telephonic b)☐ Video Conference
c)☐ Personal [copy given to: 1)☐ applicant 2)☐ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☒ No.
If Yes, brief description: _____.

Claim(s) discussed: *all pending claims*.

Identification of prior art discussed: *prior art of record*.

Agreement with respect to the claims f)☐ was reached. g)☐ was not reached. h)☒ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *Participants discussed many aspects of the application and worked together to advance prosecution of the application. The participants agreed to amend the claims and provide a supplemental amendment to place the case in a favorable condition for allowance*.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN A NON-EXTENDABLE PERIOD OF THE LONGER OF ONE MONTH OR THIRTY DAYS FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

/Michael C. Astorino/ Primary Examiner, Art Unit 3769	571-272-4723

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

———

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

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The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/437,551	05/19/2006	Bruce A. Williams	CELG-0508	3533

23377 7590 05/19/2010

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EXAMINER	
ASTORINO, MICHAEL C	
ART UNIT	**PAPER NUMBER**
3769	

MAIL DATE	DELIVERY MODE
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Interview Summary	Application No.	Applicant(s)	
	11/437,551	WILLIAMS ET AL.	
	Examiner	Art Unit	
	Michael C. Astorino	3769	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Michael C. Astorino*.

(2) *Stephanie Barbosa*.

(3)*Richard Girards*.

(4)_____.

Date of Interview: *20 April 2010*.

Type: a)☐ Telephonic b)☐ Video Conference
c)☒ Personal [copy given to: 1)☐ applicant 2)☐ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☒ No.
If Yes, brief description: _____.

Claim(s) discussed: *Independent claims*.

Identification of prior art discussed: *applied prior art*.

Agreement with respect to the claims f)☐ was reached. g)☐ was not reached. h)☒ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *Participants discussed the previous office action, the Applicant's latest response, the claims, and the prior art. No specific agreement regarding the claim was reached. The Examiner provided Applicants' representatives with general guidance with respect to the prosecution of the claims, and stated that if any issues remained in the application the Examiner would make an effort to resolve the issues by telephone*.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

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/Michael C. Astorino/ Primary Examiner, Art Unit 3769	571-272-4723

Summary of Record of Interview Requirements

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- Name of applicant
- Name of examiner
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3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/437,551	05/19/2006	Bruce A. Williams	CELG-0508	3533

23377 7590 08/12/2010

WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

EXAMINER	
RAJAN, KAI	

ART UNIT	PAPER NUMBER
3769	

MAIL DATE	DELIVERY MODE
08/12/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	11/437,551	WILLIAMS ET AL.	
	Examiner	Art Unit	
	Kai Rajan	3769	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges the response filed on May 6, 2010.

Response to Arguments

Applicant's arguments with respect to claims have been considered and are found persuasive regarding the applied prior art. As such, rejections under 35 U.S.C. 103 have been withdrawn. The Examiner agrees with Applicant's remarks of January 19, 2010 that at the very least, the applied prior art fails to disclose "providing verbal and written warnings of the risk of possible contraception failures . . ." in conjunction with a method for obtaining a prescription approval code for distribution to *male* patients.

Double Patenting

Claims 32 – 38 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 15 – 17 and 21 of copending Application No. 11/104013. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. In particular, both applications have nearly identical independent claims aside from the usage of the terms "prescription" in 11/104013 and "approval code" in the instant application. Under the broadest reasonable interpretation of the claim language in light of the specification, a "prescription" and "approval code" are equivalent since both are received by the pharmacy before a prescription is filled. Furthermore, the instant application does not distinguish in the

claims between a "prescription" and "approval code," since the claim only discloses the receipt of an "approval code" by the pharmacy.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 32 – 38 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. In particular, Applicant amended the claims on May 6, 2010 to claim a "computer readable storage medium" performing the steps of registering a patient and distributor and generating a prescription approval code. However, a computer readable medium is not a machine or apparatus, since the broadest reasonable interpretation of "computer readable medium" includes carrier waves. An example of a physical computer readable medium would be "non-transitory computer readable medium." Furthermore, the written description fails to disclose a computer readable medium "generating a prescription approval code." Therefore, for the aforementioned reasons the claims fail to recite the machine or apparatus performing essential steps of the method. Applicant is invited to make the record clear regarding how the prescription approval code is "generat[ed] via a computer readable storage medium."

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32 – 38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, the written description fails to disclose a "computer readable medium generating the prescription approval code" as claimed in claim 32. Claims 33 – 38 are rejected based on their dependency from claim 32.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32 – 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, claim 32 recites a "prescription approval code" for a prescription. It is unclear from the claim language whether the approval code is the prescription itself, since a step of receiving or generating a prescription order is not separately disclosed. Without more, the "approval code" is interpreted as the communication from a prescriber of the request for medication to be filled by a pharmacy, which is the same as a prescription. Claims 33 – 38 are rejected based on their dependency from claim 32.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kai Rajan whose telephone number is (571)272-3077. The examiner can normally be reached on Monday - Friday 9:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Henry Johnson can be reached on 571-272-4768. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kai Rajan/
Examiner, Art Unit 3769

/Henry M. Johnson, III/
Supervisory Patent Examiner, Art Unit 3769

August 10, 2010

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	11437551	WILLIAMS ET AL.
	Examiner	Art Unit
	Kai Rajan	3769

SEARCHED

Class	Subclass	Date	Examiner
600	300-301	4/08	MA
128	920	4/08	MA
705	2-4	4/08	MA
235	375	4/08	MA
	EAST Search Updated	8/10/2010	KR

SEARCH NOTES

Search Notes	Date	Examiner
IDS	4/08	MA
See parent cases	4/08	MA
EAST Inventor Search	4/08	MA
STIC Search to Find sept 1997 Transcript	4/08	MA
Spoke with TQUAS(s) regarding 101 rejection	4/08	MA
West Search Timed out, lost class and text search	4/08	MA
STIC Search	December 2008	SN
Spoke with TQAS regarding 101 and 112 2nd rejections	December 2008	SN
EAST Text Search Updated	December 2008	SN
See 11104103, and applied prior art	9/09	MA
EAST Search Updated	8/1/20100	KR

INTERFERENCE SEARCH

Class	Subclass	Date	Examiner
	Search Completed in EAST	8/2/2010	KR

/Kai Rajan/ Examiner.Art Unit 3769	

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	7176	((600/300,301) or (128/903-905,920)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2010/06/17 11:52
S2	0	(thalidomide and warning and (oral verbal) and written and prescription and approval).clm.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2010/06/17 11:55
S4	2	"6478736".pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2010/06/17 12:31
S3	2	"6478736".pn,.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2010/06/17 12:31
S5	1	S4 and heart and rate and rmr and rest $4	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2010/06/17 13:20
S6	1	S4 and (heart near2 rate) and rmr and rest $4	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2010/06/17 13:29
S7	2	"6513532".pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2010/06/17 13:31
S8	1	S7 and rest$4 and (heart near2 rate) and rmr	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2010/06/17 13:58
S9	1	S7 and rest$4 with (heart near2 rate)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2010/06/17 14:01
S10	1	S3 and rest$4 with (heart near2 rate)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2010/06/17 14:22

S11	1	(09/669125).APP.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2010/06/17 14:23
S13	1	S11 and heart near2 rate	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2010/06/17 14:24
S12	0	S11 and heart near2 rate with rest$4	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2010/06/17 14:24
S15	1	(09/685625).APP.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2010/06/17 14:27
S14	0	(09/721382).APP.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2010/06/17 14:27
S16	2	S3 and (heart near2 rate)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2010/06/17 14:29
S18	1	S7 and (heart near2 rate) and energy	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2010/06/17 14:30
S17	2	S7 and (heart near2 rate)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2010/06/17 14:30
L2	50	((JOSEPH) near2 (KAMINSKI)).INV.	US-PGPUB; USPAT	OR	ON	2010/08/02 18:56
L1	736	((BRUCE) near2 (WILLIAMS)).INV.	US-PGPUB; USPAT	OR	ON	2010/08/02 18:56

EAST Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L4	0	(thalidomide and prescription and approval and register $3 and warning and risk).clm.	USPAT; UPAD	OR	ON	2010/08/02 18:57

L3	0	(thalidomide and prescription and approval and register $3 and male and warning and risk). clm.	USPAT; UPAD	OR	ON	2010/08/02 18:57
L5	7	(thalidomide and prescription and approval and register $3 and risk).clm.	USPAT; UPAD	OR	ON	2010/08/02 18:58

8/2/2010 7:00:16 PM
C:\Documents and Settings\krajan\My Documents\EAST\Workspaces\11437551.wsp

DOCKET NO.: CELG-0508 **PATENT**
Application No.: 11/437,551
Office Action Dated: August 12, 2010

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **Bruce A. Williams**	Confirmation No.: **3533**
Application No.: **11/437,551**	Group Art Unit: **3769**
Filing Date: **May 19, 2006**	Examiner: **Kai Rajan**

For: **Methods For Delivering A Drug To A Patient While Restricting Access To The Drug By Patients For Whom The Drug May Be Contraindicated**

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

REPLY PURSUANT TO 37 CFR § 1.111

In response to the Official Action dated **August 12, 2010**, reconsideration is respectfully requested in view of the amendments and/or remarks as indicated below:

☐ **Amendments to the Specification** begin on page of this paper.

☒ **Amendments to the Claims** are reflected in the listing of the claims which begins on page 2 of this paper.

☐ **Amendments to the Drawings** begin on page of this paper and include an attached replacement sheet.

☒ **Remarks** begin on page 5 of this paper.

☐ **Request For Refund** submitted herewith.

☒ The Commissioner is hereby authorized to charge any fee deficiency, charge any additional fees, or credit any overpayment of fees, associated with this application in connection with this filing, or any future filing, submitted to the U.S. Patent and Trademark Office during the pendency of this application, to Deposit Account No. 23-3050.

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claims 1-31 (Canceled).

32. (Previously Presented) A method of treating a male patient, suffering from erythema nodosum leprosum, with thalidomide, permitting prescriptions for thalidomide to be filled by a pharmacy only after the pharmacy has retrieved an approval code for the prescription, wherein the generation of the prescription approval code comprises the following steps:

(a) via a computer readable storage medium, registering a prescriber and the pharmacy with a distributor of thalidomide;

(b) determining whether the patient is able to understand and carry out instructions;

(c) upon determination that the patient is able to carry out the instructions, providing verbal and written warnings of the hazard of taking thalidomide and exposing fetus to the drug;

(d) further providing verbal and written warnings of the risk of possible contraception failure and of the need to use barrier contraception when having sexual intercourse with women of child bearing potential;

(e) obtaining acknowledgement of said warnings from the patient;

(f) via a computer readable storage medium, registering the patient with the distributor; and

(g) upon obtaining the acknowledgement and registrations, generating via a computer readable storage medium the prescription approval code to be retrieved by the pharmacy before the prescription is filled; and

(h) upon retrieving a prescription approval code, administering thalidomide to the patient.

33. (Previously Presented) The method of claim 32, wherein the acknowledgement requires the patient's acknowledgement of one or more of the following:

(a) the understanding that thalidomide must not be taken if unprotected sex cannot be avoided;

(b) the understanding of potential birth defects;

(c) that the patient has been advised of the need for barrier contraception by the prescriber;

(d) the obligation to inform the prescriber if the patient's sexual partner is suspected of becoming or being pregnant;

(e) that thalidomide is solely for the use of the patient himself and must not be shared with any other person;

(f) that the patient has read the information brochure or viewed the information film on thalidomide;

(g) that the semen or blood must not be donated during the thalidomide treatment;

(h) that all of the patient's inquiries regarding thalidomide treatment have been answered by the prescribing physician; or

(i) the patient's understanding that participation in a survey and patient registry is required during the thalidomide treatment.

34. (Previously Presented) The method of claim 32 further comprising providing the patient, prior to generation of the approval code, with warnings of the side effects associated with administration of thalidomide, wherein said side effects are non-teratogenic side effects.

35. (Previously Presented) The method of claim 32 further comprising obtaining a written authorization by the prescriber prior to generation of the approval code.

36. (Previously Presented) The method of claim 32, wherein the prescription approval code is retrieved from a computer readable storage medium.

37. (Previously Presented) The method of claim 32, wherein the acknowledgement is a written informed consent.

38. (Previously Presented) The method of claim 37, wherein the written informed consent is registered in the medium prior to generation of the prescription approval code.

REMARKS

Claims 32-38 are pending. No claim amendments have been made. Applicants note that the rejections under 35 U.S.C. § 103 have been withdrawn.

Rejection under 35 U.S.C. § 101

Claims 32-38 stand rejected under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter. The Applicants note that this rejection has been previously applied and withdrawn by the Office during prosecution. Nevertheless, it appears that the Office is now rigidly applying the "machine or apparatus" test that was rejected by the United States Supreme Court in *In re Bilski*. "The Court is unaware of any ordinary, contemporary, common meaning of "process" that would require it to be tied to a machine or the transformation of an article." *Bilski v. Kappos*, 130 S. Ct. 3218, 3226 (2010).

The Office is required to make the subject matter eligibility determination with respect to the claims as a whole to evaluate whether the claims are patent-eligible or whether the abstract idea exception renders the claim ineligible. MPEP 2106. ("[W]hen evaluating the scope of a claim, every limitation in the claim must be considered. USPTO personnel may not dissect a claimed invention into discrete elements and then evaluate the elements in isolation. Instead, the claim as a whole must be considered.")

Here, the Office alleges that "computer readable storage medium" does not recite a machine or apparatus as the phrase can be interpreted to include carrier waves. The Supreme Court rejected the rigid machine or apparatus test and required a more comprehensive evaluation of the subject matter of the entire claim, in light of the specification and claims. Yet the Office appears to be focused on only one limitation of the claims – the generation of the approval code via a computer readable storage medium – which is improper. The Office is required to consider the claim in its entirety to determine whether it is directed to patentable subject matter.

Not only has the Office failed to consider the claims in their entirety, the Office has unreasonably interpreted "computer readable storage medium" be to carrier waves. The skilled person, reading the specification and claims in their entirety, would understand that "computer readable storage medium" includes physical components and is not simply carrier waves.

Indeed, with regard to the "generating a prescription approval code step," paragraph [0047] of the specification recites that the "registered pharmacy consult the computer readable medium to retrieve a prescription approval code before dispensing the drug to the patient." Clearly, the pharmacy cannot consult carrier waves to retrieve a code.

Moreover, the claimed invention results in the retrieval of a prescription approval code and the administration of thalidomide to the patient, which is clearly within the scope of what is patentable subject matter under 35 U.S.C. § 101.

The claims are not directed to laws of nature, physical phenomena, or abstract ideas and therefore do encompass statutory subject matter pursuant to the law as recently clarified by the Supreme Court. *Bilski,* 130 S. Ct. at 3225. ("The Courts' precedents provide three specific exceptions to § 101's broad patent eligibility principles: "laws of nature, physical phenomena, and abstract ideas."). Withdrawal of the rejection is requested.

Rejections under 35 U.S.C. § 112

Claims 32-38 stand rejected under 35 U.S.C. § 112, first paragraph, as alleged failing to comply with the written description requirement. The Office alleges that the specification fails to disclose "a "computer readable medium generating the prescription approval code." The Applicants disagree and assert that the specification clearly describes that the prescription approval code is generated by the computer readable medium.

MPEP 608.02(g) states that the specification "should provide clear support ***or*** antecedent basis for the claims." (emphasis added). As such, there is no strict requirement that verbatim antecedent support for claim recitations, *i.e.*, the same exact words, be provided in the specification. Rather, it is sufficient that the claimed feature be clearly supported by the specification. Here, the Office alleges that there is no support for a "computer readable medium generating the prescription approval code." The Applicants note that paragraph [0047] states that the "registered pharmacy consult the computer readable medium to retrieve a prescription approval code before dispending the drug to the patient." The skilled person would understand that the specification clearly supports that the approval code has been retrieved from the computer readable storage medium because the computer readable storage medium has

generated the approval code. Paragraph [0047] describes that in order to generate the prescription approval code, the prescriber, the pharmacy, the patient, etc., must first be registered in the storage medium. The generation of the prescription approval code may further require the registration in the storage medium of additional sets of information such as periodic surveys and the results of diagnostic tests. *Id.* The specification clearly supports that the prescription approval code is retrieved from the computer readable storage medium that generated the code. Withdrawal of the rejection is requested.

Claims 32-38 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The Office alleges that the specification does not distinguish "prescription approval code" from "prescription." The Applicants disagree.

According to the specification, the prescription can be generated by the prescriber simply once the prescriber is registered in the computer readable storage medium. Specification at paragraph [0019]. In contrast, according to the invention, prior to filling the prescription, an approval code must be obtained. While a prescription can be written once the prescriber is registered, an approval code is not provided unless the prescriber, the pharmacy, the patient, and the patient's informed consent have been registered in the storage medium. Specification at paragraph [0047]. Moreover, while a prescription might be provided, an approval code might not be generated, hence preventing the dispensing of the drug, if the proper registrations have not been registered. *Id.*

The "prescription" and "prescription approval code" have different meanings, as set forth in the specification as originally filed. Withdrawal of the rejection is requested.

Double Patenting

Claims 32-38 stand provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as that of claims 15-17 and 21 of U.S. Application No. 11/104,013. The Office alleges that the claims of the present application have nearly identical independent claims aside from the usage of the terms "prescription" in 11/104,013 and "approval code" in the present application. The Applications disagree that the two applications have identical claims. As described above,

"prescription" and "prescription approval code" have difference meanings as described in the specification. Withdrawal of the rejection is requested.

The Applicants assert that claims 32-38 are in condition for allowance. An early notice that that effect is earnestly requested.

Date: November 9, 2010

/Stephanie A. Barbosa/
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Electronic Acknowledgement Receipt

EFS ID:	8796535
Application Number:	11437551
International Application Number:	
Confirmation Number:	3533
Title of Invention:	Methods for delivering a drug to a patient while restricting access to the drug by patients for whom the drug may be contraindicated
First Named Inventor/Applicant Name:	Bruce A. Williams
Customer Number:	23377
Filer:	Stephanie A. Barbosa/D. McCarty
Filer Authorized By:	Stephanie A. Barbosa
Attorney Docket Number:	CELG-0508
Receipt Date:	09-NOV-2010
Filing Date:	19-MAY-2006
Time Stamp:	10:34:31
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	CELG-0508-Transmittal-reply-to-08-12-10.PDF	281566 7e93ac5498ef5beefe91ad659d3f732a3f0966c3	no	2

Warnings:	
Information:	

2		CELG-0508-Reply-to-08-12-10.PDF	101426 39d11fcfdf6459675d0a1c1293df3e75aac49399	yes	8

Multipart Description/PDF files in .zip description

Document Description	Start	End
Amendment/Req. Reconsideration-After Non-Final Reject	1	1
Claims	2	4
Applicant Arguments/Remarks Made in an Amendment	5	8

Warnings:

Information:

Total Files Size (in bytes):	382992

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National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

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PTO/SB/21 (07-09)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission	

Application Number	11/437,551
Filing Date	May 19, 2006
First Named Inventor	Bruce A. Williams
Art Unit	3769
Examiner Name	Kai Rajan
Attorney Docket Number	CELG-0508

ENCLOSURES (*Check all that apply*)

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☑ Amendment/Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Reply to Missing Parts/ Incomplete Application
  - ☐ Reply to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s) _____
  - ☐ Landscape Table on CD
- ☐ After Allowance Communication to TC
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- ☐ Proprietary Information
- ☐ Status Letter
- ☐ Other Enclosure(s) (please Identify below):

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Woodcock Washburn, LLP		
Signature	/Stephanie A. Barbosa/		
Printed name	Stephanie A. Barbosa		
Date	November 9, 2010	Reg. No.	51430

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PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 11/437,551	Filing Date 05/19/2006	☐ To be Mailed

APPLICATION AS FILED – PART I

	(Column 1)	(Column 2)	SMALL ENTITY ☐		OR	OTHER THAN SMALL ENTITY	
FOR	NUMBER FILED	NUMBER EXTRA	RATE ($)	FEE ($)		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT 02/25/2010	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	* 23	Minus	** 24	= 0	X $ =		OR	X $52=	0
Independent (37 CFR 1.16(h))	* 5	Minus	***5	= 0	X $ =		OR	X $220=	0
☐ Application Size Fee (37 CFR 1.16(s))									
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
					TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	0

AMENDMENT 11/09/2010	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)		RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	* 7	Minus	** 20	= 0	X $ =		OR	X $52 =	0
Independent (37 CFR 1.16(h))	* 1	Minus	*** 3	= 0	X $ =		OR	X $220 =	0
☐ Application Size Fee (37 CFR 1.16(s))									
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
					TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	0

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

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Legal Instrument Examiner:
/GLENN BURNS JR/

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/437,551	05/19/2006	Bruce A. Williams	CELG-0508	3533

23377 7590 11/19/2010

WOODCOCK WASHBURN LLP
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2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

EXAMINER	
RAJAN, KAI	

ART UNIT	PAPER NUMBER
3769	

NOTIFICATION DATE	DELIVERY MODE
11/19/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

eofficemonitor@woodcock.com

Office Action Summary	Application No.	Applicant(s)	
	11/437,551	WILLIAMS ET AL.	
	Examiner	Art Unit	
	Kai Rajan	3769	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges the response filed on November 9, 2010.

Response to Arguments

Applicant's arguments with respect to claims have been considered and are not persuasive. Arguments are addressed below within each rejection.

Applicant is invited to request an interview to discuss these rejections and suggestions to advance prosecution of the case.

Double Patenting

Claims 32 – 38 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 15 – 17 and 21 of copending Application No. 11/104013. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications have nearly identical independent claims aside from the usage of the terms "prescription" in 11/104013 and "approval code" in the instant application. Under the broadest reasonable interpretation of the claim language in light of the specification, a “prescription” and “approval code” are equivalent since both are received by the pharmacy before a prescription is filled. Furthermore, the instant application does not distinguish ***in the claims*** between a "prescription" and "approval code," since the claim only discloses the receipt of an “approval code” by the pharmacy.

In the remarks filed November 9, 2010, Applicant contends the terms “prescription" and “approval code” are described separately in the specification. Upon review of the specification, the Examiner agrees that an approval code is a form of authorization for a submitted prescription. However, the claim only recites the receipt of an "approval code.” Similarly, claim 15 of the copending Application 11/104013 recites the receipt of a prescription, which is described throughout the specification to indicate the authorization of filling that prescription. It is submitted that the term "prescription" as used in Application 11/104013 is equivalent to the "approval code" in the instant application. Both claims of both applications only require a single receipt of authorization to fill a prescription. Therefore, the claims remain provisionally rejected.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 32 – 38 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. In particular, the claims recite “computer readable storage medium" performing the steps of registering a patient and distributor and generating a prescription approval code. However, a computer readable medium is not a machine or apparatus, since the broadest reasonable interpretation of “computer readable medium” includes carrier waves. An example of a physical computer readable medium would be “non-transitory computer readable medium." Furthermore, the written description fails to disclose a computer readable medium "generating a prescription approval code." Therefore, for the aforementioned reasons the claims fail to recite the machine or apparatus performing essential steps of the

method. Applicant is invited to make the record clear regarding how the prescription approval code is "generat[ed] via a computer readable storage medium."

Applicant's remarks of November 9, 2010 contend that the claims are patentable in light of recent *Bilski* holdings (130 S. Ct. 3218 (2010)). The Examiner disagrees.

First, the Examiner notes that a strict machine / apparatus test is not used to evaluate the claims, and the claims are evaluated as a whole. However, essential steps of the method other than mere data gathering or other insignificant steps must be tied to a machine or transformation. Regarding claim 32, all of the method steps may be interpreted as mental steps or steps performed by hand by a human. The only apparatus supposedly recited is a "computer readable medium," which could be interpreted as a sheet of paper on which approval codes or registration information is written. Since none of the steps are tied to any particular machine or apparatus, let alone the essential step of generating an approval code as previously noted by the Examiner, the claims are directed to non-statutory subject matter. An additional factor weighing against patentability is that the mechanism by which the steps are implemented is subjective, such as the step of "obtaining acknowledgement of said warnings" or "determining whether the patient is able to understand and carry out instructions."

Even if a "computer readable medium" performed the step of "generating . . . [an] approval code," the broadest reasonable interpretation of "computer readable medium" includes carrier waves. One explicit example of this interpretation is shown in Mitchell et al. U.S. Patent No. 2005/0235345 A1 (referenced as extrinsic evidence but not relied upon as prior art to the instant case). In paragraphs 0020 - 0021, Mitchell et al. discusses different types of storage and communications media known in the art, and states that "computer readable media" can include

the types mentioned therein. Therefore, unless Applicant's specification explicitly defines the types of media used, the broadest reasonable interpretation applies. To overcome such a rejection, Applicant may amend the claims to read "a *non-transitory* computer readable medium."

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32 – 38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, the written description fails to disclose a “computer readable medium generating the prescription approval code” as claimed in claim 32. Claims 33 – 38 are rejected based on their dependency from claim 32.

In the response filed November 9, 2010, Applicant contends paragraph 0047 provides support for the claim limitation. The Examiner disagrees. The paragraph merely states "depending upon the risk group assignment, generation of the prescription approval code may further require the registration in the storage medium of the additional sets of information . . .” The remainder of the paragraph discusses retrieving an approval code stored in the medium. This in no way supports the conclusion that the code is *generated* by the computer readable

medium. The code may be input by a physician once the necessary data is registered in the computer readable medium. The Examiner agrees with Applicant's remark that the claims do not have to mirror the specification verbatim, however in this case the specification only supports the storage on and retrieval from a computer readable medium. At least paragraph 0047 is completely silent regarding how the code is generated. Therefore, the claim limitation remains rejected.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32 – 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, claim 32 recites a "prescription approval code" for a prescription. It is unclear from the claim language whether the approval code is the prescription itself, since a step of receiving or generating a prescription order is not separately disclosed ***in the claims***. Without more, the "approval code" is interpreted as the communication from a prescriber of the request for medication to be filled by a pharmacy, which is the same as a prescription. Only an "approval code" is received in the claims, as opposed to separate receipts of a "prescription" followed by an "approval code." This renders the claims indefinite, since the definition of a prescription itself is "a written direction for a therapeutic or corrective agent, (Merriam – Webster)" which appears to be the same as an "approval code." Claims 33 – 38 are rejected based on their dependency from claim 32.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kai Rajan whose telephone number is (571)272-3077. The examiner can normally be reached on Monday - Friday 9:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Henry Johnson can be reached on 571-272-4768. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kai Rajan/
Examiner, Art Unit 3769

/Henry M. Johnson, III/
Supervisory Patent Examiner, Art Unit 3769

November 12, 2010

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1	(11/104013).APP.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2010/11/12 12:12
L2	7529	((600/300,301) or (128/903-905,920)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2010/11/12 12:30
L3	7529	L2	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2010/11/12 12:30
L4	2033	l3 and @ad<"20001023"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2010/11/12 12:31
L5	13	l4 and prescription with (approved approval authorized authorization)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2010/11/12 12:32
L6	0	l5 and thalidomide	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2010/11/12 12:33

EAST Search History (Interference)

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11/12/2010 12:40:30 PM
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Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	11437551	WILLIAMS ET AL.
	Examiner	Art Unit
	Kai Rajan	3769

SEARCHED

Class	Subclass	Date	Examiner
600	300-301	4/08	MA
128	920	4/08	MA
705	2-4	4/08	MA
235	375	4/08	MA
	EAST Search Updated	8/10/2010	KR
	EAST Search Updated	11/12/2010	KR

SEARCH NOTES

Search Notes	Date	Examiner
IDS	4/08	MA
See parent cases	4/08	MA
EAST Inventor Search	4/08	MA
STIC Search to Find sept 1997 Transcript	4/08	MA
Spoke with TQUAS(s) regarding 101 rejection	4/08	MA
West Search Timed out, lost class and text search	4/08	MA
STIC Search	December 2008	SN
Spoke with TQAS regarding 101 and 112 2nd rejections	December 2008	SN
EAST Text Search Updated	December 2008	SN
See 11104103, and applied prior art	9/09	MA
EAST Search Updated	8/1/20100	KR
EAST Search Updated (text search within classes)	11/12/2010	KR

INTERFERENCE SEARCH

Class	Subclass	Date	Examiner
	Search Completed in EAST	8/2/2010	KR

/Kai Rajan/ Examiner.Art Unit 3769	

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/437,551	05/19/2006	Bruce A. Williams	CELG-0508	3533

23377 7590 02/08/2011

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2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

EXAMINER	
RAJAN, KAI	

ART UNIT	PAPER NUMBER
3769	

NOTIFICATION DATE	DELIVERY MODE
02/08/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

eofficemonitor@woodcock.com

Interview Summary	Application No.	Applicant(s)	
	11/437,551	WILLIAMS ET AL.	
	Examiner	Art Unit	
	Kai Rajan	3769	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Kai Rajan*.

(2) *Stephanie A. Barbosa*.

(3) *Henry Johnson*.

(4) _____.

Date of Interview: *01 February 2011*.

Type: a)☒ Telephonic b)☐ Video Conference
c)☐ Personal [copy given to: 1)☐ applicant 2)☐ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☒ No.
If Yes, brief description: _____.

Claim(s) discussed: *32*.

Identification of prior art discussed: *n/a*.

Agreement with respect to the claims f)☒ was reached. g)☐ was not reached. h)☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *Examiners and Applicant's Representative discussed the previous rejection, and suggestions to overcome 35 U.S.C. 101 and 112 rejections, as well as the double patenting rejection previously made*.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN A NON-EXTENDABLE PERIOD OF THE LONGER OF ONE MONTH OR THIRTY DAYS FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

/Kai Rajan/ Examiner, Art Unit 3769	/Henry M. Johnson, III/ Supervisory Patent Examiner, Art Unit 3769

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:
- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:
1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

DOCKET NO.: CELG-0508 **PATENT**
Application No.: 11/437,551
Office Action Dated: November 19,2010

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **Bruce A. Williams**	Confirmation No.: **3533**
Application No.: **11/437,551**	Group Art Unit: **3769**
Filing Date: **May 19, 2006**	Examiner: **Kai Rajan**

For: **Methods For Delivering A Drug To A Patient While Restricting Access To The Drug By Patients For Whom The Drug May Be Contraindicated**

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

REPLY PURSUANT TO 37 CFR § 1.116

In response to the Official Action dated **November 19,2010**, reconsideration is respectfully requested in view of the amendments and/or remarks as indicated below:

☐ **Amendments to the Specification** begin on page of this paper.

☒ **Amendments to the Claims** are reflected in the listing of the claims which begins on page 2 of this paper.

☐ **Amendments to the Drawings** begin on page of this paper and include an attached replacement sheet.

☒ **Remarks** begin on page 5 of this paper.

☒ The Commissioner is hereby authorized to charge any fee deficiency, charge any additional fees, or credit any overpayment of fees, associated with this application in connection with this filing, or any future filing, submitted to the U.S. Patent and Trademark Office during the pendency of this application, to Deposit Account No. 23-3050.

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claims 1-31 (Canceled).

32. (Currently Amended) A method of treating a male patient, suffering from erythema nodosum leprosum, with thalidomide, by permitting prescriptions for thalidomide to be filled by a pharmacy only after the pharmacy has retrieved ~~an~~ a prescription approval code for the prescription, comprising ~~wherein the generation of the prescription approval code comprises~~ the following steps:

(a) via a non-transitory computer readable storage medium, registering a prescriber and the pharmacy with a distributor of thalidomide;

(b) determining whether the patient is able to understand and carry out instructions;

(c) upon determination that the patient is able to carry out the instructions, providing verbal and written warnings of the hazard of taking thalidomide and exposing fetus to the drug;

(d) further providing verbal and written warnings of the risk of possible contraception failure and of the need to use barrier contraception when having sexual intercourse with women of child bearing potential;

(e) obtaining acknowledgement of said warnings from the patient;

(f) providing the prescription for thalidomide to the patient from the prescriber;

(g)~~(f)~~ via a non-transitory computer readable storage medium, registering the patient with the distributor; ~~and~~

(h)~~(g)~~ upon obtaining the acknowledgement and registrations, generating the prescription approval code, and via a non-transitory computer readable storage medium, retrieving the prescription approval code ~~to be retrieved~~ by the pharmacy before the prescription is filled; and

(i)~~(h)~~ upon retrieving [[a]] the prescription approval code, administering thalidomide to the patient.

33. (Previously Presented) The method of claim 32, wherein the acknowledgement requires the patient's acknowledgement of one or more of the following:

(a) the understanding that thalidomide must not be taken if unprotected sex cannot be avoided;

(b) the understanding of potential birth defects;

(c) that the patient has been advised of the need for barrier contraception by the prescriber;

(d) the obligation to inform the prescriber if the patient's sexual partner is suspected of becoming or being pregnant;

(e) that thalidomide is solely for the use of the patient himself and must not be shared with any other person;

(f) that the patient has read the information brochure or viewed the information film on thalidomide;

(g) that the semen or blood must not be donated during the thalidomide treatment;

(h) that all of the patient's inquiries regarding thalidomide treatment have been answered by the prescribing physician; or

(i) the patient's understanding that participation in a survey and patient registry is required during the thalidomide treatment.

34. (Previously Presented) The method of claim 32 further comprising providing the patient, prior to generation of the approval code, with warnings of the side effects associated with administration of thalidomide, wherein said side effects are non-teratogenic side effects.

35. (Previously Presented) The method of claim 32 further comprising obtaining a written authorization by the prescriber prior to generation of the approval code.

36. (Canceled)

37. (Previously Presented) The method of claim 32, wherein the acknowledgement is a written informed consent.

REMARKS

The undersigned thanks Examiners Rajan and Johnson for the courtesy of the telephonic interview that was held on February 1, 2011. Claim 32 was discussed in light of the outstanding rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112. The obviousness-type double patenting rejection over U.S. App. No. 11/104013, now U.S. 7,874,984, was also discussed. It was agreed that amending the term "computer readable storage medium" to "non-transitory computer readable storage medium" would obviate the rejection under 35 U.S.C. § 101. Claim amendments discussed during that interview are presented here. Favorable consideration of the amendments and an indication of the allowability of claims 32-35 and 37 is requested.

Rejection under 35 U.S.C. § 101

Claims 32-38 stand rejected under 35 U.S.C. 101 as allegedly directed to non-statutory subject matter. The applicants disagree that the "broadest reasonable interpretation of 'computer readable medium' includes carrier waves." The applicants further disagree with the Office's allegation that the claims "fail to recite the machine or apparatus performing essential steps of the method." The Office has suggested that the rejection can be overcome by amending the claims to recite "a non-transitory computer readable storage medium." While the applicants do not agree that such an amendment is required in order to convey to the skilled person, reading the claims in view of the specification, that the claims are tied to a machine or apparatus, the claims have been so amended in order to advance the present application to allowance. Reconsideration and withdrawal of the rejection is requested.

Rejection under 35 U.S.C. § 112

Claims 32-28 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement for allegedly failing to disclose a "computer readable medium generating the prescription approval code." While the applicants maintain the prior arguments that the claims comply with 35 U.S.C. § 112, first paragraph, the claims have been amended to recite "generating a prescription approval code." *See* Specification at

paragraph [0047]. The applicants expressly reserve the right to file the canceled subject matter in one or more continuing or divisional applications.

Claims 32-38 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The Office alleges that the claims are unclear as to whether the "prescription" is a separate limitation from the "prescription approval code." As previously argued, it is the applicants' assertion that the claims are not unclear and that one skilled in the art would readily understand the "prescription" to be a distinct limitation from the "prescription approval code." Nevertheless, in order to advance the application to allowance, the claims have been amended to expressly provide for the step of providing the prescription for thalidomide to the patient from the prescriber. Reconsideration and withdrawal of the rejection is requested.

Obviousness-type double patenting

Claims 32-28 stand rejected as allegedly unpatentable over the claims of U.S. App. No. 11/104,013, now U.S. 7,874,984. The applicants disagree and request reconsideration and withdrawal of the rejection. The claims of U.S. 7,874,984 describe the generation of a prescription. A prescription is generated, according to U.S. 7,874,984, only after acknowledgements and registrations are obtained. Upon obtaining those acknowledgements and registrations, a computer readable storage medium generates a prescription to be received by the pharmacy before thalidomide is distributed.

In contrast to the claims of U.S. 7,874,984, the present invention is not directed to the generation of a prescription. In the present claims, the prescriber provides the prescription to the patient; it is not generated via a computer readable storage medium. Moreover, the present claims require the retrieval of an approval code from a computer readable storage medium prior to filling the prescription that has already been provided to the patient by the prescriber. The claims of U.S. 7,874,984 do not include such a limitation.

The present claims are patentably distinct from the claims of U.S. 7,874,984; therefore, the present claims do not unjustly extend the patent term of U.S. 7,874,984. As such, the obviousness-type double patenting rejection is not proper and should be withdrawn.

Claims 32-35 and 37 are in condition for allowance. An early notice to that effect is, therefore, earnestly solicited.

Date: February 25, 2011

/Stephanie A. Barbosa/
Stephanie A. Barbosa
Registration No. 51,430

Woodcock Washburn LLP
Cira Centre
2929 Arch Street, 12th Floor
Philadelphia, PA 19104-2891
Telephone: (215) 568-3100
Facsimile: (215) 568-3439

Electronic Patent Application Fee Transmittal

Application Number:	11437551
Filing Date:	19-May-2006
Title of Invention:	Methods for delivering a drug to a patient while restricting access to the drug by patients for whom the drug may be contraindicated
First Named Inventor/Applicant Name:	Bruce A. Williams
Filer:	Stephanie A. Barbosa/D. McCarty
Attorney Docket Number:	CELG-0508

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Extension - 1 month with $0 paid	1251	1	130	130

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
			Total in USD ($)	**130**

Electronic Acknowledgement Receipt

EFS ID:	9532566
Application Number:	11437551
International Application Number:	
Confirmation Number:	3533
Title of Invention:	Methods for delivering a drug to a patient while restricting access to the drug by patients for whom the drug may be contraindicated
First Named Inventor/Applicant Name:	Bruce A. Williams
Customer Number:	23377
Filer:	Stephanie A. Barbosa/D. McCarty
Filer Authorized By:	Stephanie A. Barbosa
Attorney Docket Number:	CELG-0508
Receipt Date:	25-FEB-2011
Filing Date:	19-MAY-2006
Time Stamp:	12:03:09
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$130
RAM confirmation Number	11733
Deposit Account	233050
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	CELG-0508-Transmittal-reply-to-11-19-10.PDF	276468 60299e87bd447e31701a8cb66e10935c5e221602	no	2
Warnings:					
Information:					
2	Extension of Time	CELG-0508-Petition-for-Extension-of-time.PDF	327802 c256b7156cb62262477218c6ed26c7f59aec78a1	no	2
Warnings:					
Information:					
3		CELG-0508-Reply-to-11-19-10.PDF	86564 7346b3c2b601bdf7ae7b8c28e5b3714860e4390f	yes	7

Multipart Description/PDF files in .zip description

Document Description	Start	End
Amendment After Final	1	1
Claims	2	4
Applicant Arguments/Remarks Made in an Amendment	5	7

Warnings:					
Information:					
4	Fee Worksheet (PTO-875)	fee-info.pdf	30367 dcc78ca25515c47e4147e60703a6ae71107f43a9	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	721201		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/21 (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission

Application Number	11/437,551
Filing Date	May 19, 2006
First Named Inventor	Bruce A. Williams
Art Unit	3769
Examiner Name	Kai Rajan
Attorney Docket Number	CELG-0508

ENCLOSURES (*Check all that apply*)

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☑ Amendment/Reply
  - ☑ After Final
  - ☐ Affidavits/declaration(s)
- ☑ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Reply to Missing Parts/ Incomplete Application
  - ☐ Reply to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s) _____
  - ☐ Landscape Table on CD
- ☐ After Allowance Communication to TC
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- ☐ Proprietary Information
- ☐ Status Letter
- ☐ Other Enclosure(s) (please Identify below):

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Woodcock Washburn, LLP		
Signature	/Stephanie A. Barbosa/		
Printed name	Stephanie A. Barbosa		
Date	February 25, 2011	Reg. No.	51430

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

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Typed or printed name		Date	

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

PTO/SB/22 (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARMENT OF COMMERCE

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a) **FY 2009** (*Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).*)	Docket Number (Optional) CELG-0508
Application Number 11/437,551	Filed May 19, 2006
For Methods For Delivering A Drug To A Patient While Restricting Access To The Drug By Patients For Whor	
Art Unit 3769	Examiner Kai Rajan

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

		Fee	Small Entity Fee	
☑	One month (37 CFR 1.17(a)(1))	$130	$65	$ 130.00
☐	Two months (37 CFR 1.17(a)(2))	$490	$245	$
☐	Three months (37 CFR 1.17(a)(3))	$1110	$555	$
☐	Four months (37 CFR 1.17(a)(4))	$1730	$865	$
☐	Five months (37 CFR 1.17(a)(5))	$2350	$1175	$

☐ Applicant claims small entity status. See 37 CFR 1.27.

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☑ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 233050.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest. See 37 CFR 3.71.
Statement under 37 CFR 3.73(b) is enclosed (Form PTO/SB/96).

☑ attorney or agent of record. Registration Number 51,430

☐ attorney or agent under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

/Stephanie A. Barbosa/ — Signature

February 25, 2011 — Date

Stephanie A. Barbosa — Typed or printed name

215-568-3100 — Telephone Number

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below.

☑ Total of 1 forms are submitted.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
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9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

PTO/SB/06 (07-06)
Approved for use through 1/31/2007. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number	Filing Date	☐ To be Mailed
11/437,551	05/19/2006	

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE ($)	SMALL ENTITY FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT	02/25/2011	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	SMALL ENTITY ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 5	Minus	** 24	= 0	X $ =		OR	X $52=	0
	Independent (37 CFR 1.16(h))	* 1	Minus	***5	= 0	X $ =		OR	X $220=	0
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	0

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	SMALL ENTITY ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =		OR	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =		OR	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

Legal Instrument Examiner:
/LASHAWN MORGAN/

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
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NOTICE OF ALLOWANCE AND FEE(S) DUE

23377 7590 04/26/2011
WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

EXAMINER
RAJAN, KAI

ART UNIT	PAPER NUMBER
3769	

DATE MAILED: 04/26/2011

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/437,551	05/19/2006	Bruce A. Williams	CELG-0508	3533

TITLE OF INVENTION: METHODS FOR DELIVERING A DRUG TO A PATIENT WHILE RESTRICTING ACCESS TO THE DRUG BY PATIENTS FOR WHOM THE DRUG MAY BE CONTRAINDICATED

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1510	$300	$0	$1810	07/26/2011

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

23377 7590 04/26/2011
WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/437,551	05/19/2006	Bruce A. Williams	CELG-0508	3533

TITLE OF INVENTION: METHODS FOR DELIVERING A DRUG TO A PATIENT WHILE RESTRICTING ACCESS TO THE DRUG BY PATIENTS FOR WHOM THE DRUG MAY BE CONTRAINDICATED

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1510	$300	$0	$1810	07/26/2011

EXAMINER	ART UNIT	CLASS-SUBCLASS
RAJAN, KAI	3769	600-300000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:
❑ Issue Fee
❑ Publication Fee (No small entity discount permitted)
❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
❑ A check is enclosed.
❑ Payment by credit card. Form PTO-2038 is attached.
❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
❑ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.
❑ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
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11/437,551	05/19/2006	Bruce A. Williams	CELG-0508	3533

23377 7590 04/26/2011

WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

EXAMINER	
RAJAN, KAI	

ART UNIT	PAPER NUMBER
3769	

DATE MAILED: 04/26/2011

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 99 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 99 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No.	Applicant(s)	
	11/437,551	WILLIAMS ET AL.	
	Examiner	Art Unit	
	Kai Rajan	3769	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the response filed February 25, 2011*.

2. ☒ The allowed claim(s) is/are *32-35 and 37*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☐ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

/Kai Rajan/ Examiner, Art Unit 3769	/Henry M. Johnson, III/ Supervisory Patent Examiner, Art Unit 3769

REASONS FOR ALLOWANCE

The following is an examiner's statement of reasons for allowance: The prior art of record alone or in combination fails to disclose generating an approval code for a prescription of thalidomide upon receiving acknowledgement of warnings and health risks from a male patient.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kai Rajan whose telephone number is (571)272-3077. The examiner can normally be reached on Monday - Friday 9:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Henry Johnson can be reached on 571-272-4768. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kai Rajan/
Examiner, Art Unit 3769

/Henry M. Johnson, III/
Supervisory Patent Examiner, Art Unit 3769

March 2, 2011

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	11437551	WILLIAMS ET AL.
	Examiner	**Art Unit**
	Kai Rajan	3769

SEARCHED

Class	Subclass	Date	Examiner
600	300-301	4/08	MA
128	920	4/08	MA
705	2-4	4/08	MA
235	375	4/08	MA
	EAST Search Updated	8/10/2010	KR
	EAST Search Updated	11/12/2010	KR
	EAST Search Updated	3/2/2011	KR

SEARCH NOTES

Search Notes	Date	Examiner
IDS	4/08	MA
See parent cases	4/08	MA
EAST Inventor Search	4/08	MA
STIC Search to Find sept 1997 Transcript	4/08	MA
Spoke with TQUAS(s) regarding 101 rejection	4/08	MA
West Search Timed out, lost class and text search	4/08	MA
STIC Search	December 2008	SN
Spoke with TQAS regarding 101 and 112 2nd rejections	December 2008	SN
EAST Text Search Updated	December 2008	SN
See 11104103, and applied prior art	9/09	MA
EAST Search Updated	8/1/20100	KR
EAST Search Updated (text search within classes)	11/12/2010	KR
EAST Search Updated	3/2/2011	KR

INTERFERENCE SEARCH

Class	Subclass	Date	Examiner
	Search Completed in EAST	3/2/2011	KR

/Kai Rajan/ Examiner.Art Unit 3769	

Issue Classification

Application/Control No.	Applicant(s)/Patent Under Reexamination
11437551	WILLIAMS ET AL.
Examiner	**Art Unit**
Kai Rajan	3769

ORIGINAL		INTERNATIONAL CLASSIFICATION														
CLASS	SUBCLASS	CLAIMED									NON-CLAIMED					
600	300	A	6	1	B	5 / 00 (2006.01.01)										

CROSS REFERENCE(S)					
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)				
128	920				
705	3				
235	375				

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☒ T.D. ☐ R.1.47

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
	1		17	2	33		49								
	2		18	3	34		50								
	3		19	4	35		51								
	4		20		36		52								
	5		21	5	37		53								
	6		22		38		54								
	7		23		39										
	8		24		40										
	9		25		41										
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	11		27		43										
	12		28		44										
	13		29		45										
	14		30		46										
	15		31		47										
	16	1	32		48										

/Kai Rajan/ Examiner.Art Unit 3769 (Assistant Examiner)	3/2/2011 (Date)	**Total Claims Allowed:** 5
/Henry M Johnson, III/ Supervisory Patent Examiner.Art Unit 3769 (Primary Examiner)	03/04/2011 (Date)	O.G. Print Claim(s) 1 O.G. Print Figure n/a

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BIB DATA SHEET

CONFIRMATION NO. 3533

SERIAL NUMBER	FILING or 371(c) DATE RULE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
11/437,551	05/19/2006	600	3769	CELG-0508

APPLICANTS

Bruce A. Williams, Flemington, NJ;
Joseph K. Kaminski, Hampton, NJ;

**** CONTINUING DATA ***************************

This application is a CON of 11/028,144 01/03/2005 PAT 7,141,018
which is a CON of 10/762,880 01/22/2004 PAT 6,869,399
which is a CON of 10/383,275 03/07/2003 PAT 6,755,784
which is a CON of 09/965,155 09/27/2001 PAT 6,561,977
which is a CON of 09/694,217 10/23/2000 PAT 6,315,720

**** FOREIGN APPLICATIONS ***************************

**** IF REQUIRED, FOREIGN FILING LICENSE GRANTED ****

06/09/2006

Foreign Priority claimed ☐ Yes ☑ No 35 USC 119(a-d) conditions met ☐ Yes ☑ No Verified and Acknowledged /KAI RAJAN/ Examiner's Signature	☐ Met after Allowance Initials	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
		NJ	0	5	1

ADDRESS

WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891
UNITED STATES

TITLE

Methods for delivering a drug to a patient while restricting access to the drug by patients for whom the drug may be contraindicated

FILING FEE RECEIVED		
1620	FEES: Authority has been given in Paper No._____ to charge/credit DEPOSIT ACCOUNT No._____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L4	2	(09/964068).APP.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2011/03/02 20:29
L5	2	(09/965155).APP.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2011/03/02 20:32
L7	2	(10/383655).APP.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2011/03/02 20:33
L6	2	(10/383275).APP.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2011/03/02 20:33
L8	2	(10/383665).APP.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2011/03/02 20:34
L10	2	(11/028144).APP.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2011/03/02 20:35
L9	2	(10/762880).APP.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2011/03/02 20:35
L11	1	(11/999367).APP.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2011/03/02 20:36
L17	13	L16	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2011/03/02 21:41
L16	13	L15 and prescription with (approved approval authorized authorization)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2011/03/02 21:41

L15	2033	L14 and @ad<"20001023"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2011/03/02 21:41
L14	7739	L13	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2011/03/02 21:41
L13	7739	((600/300,301) or (128/903-905,920)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2011/03/02 21:41

EAST Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L2	36	(thalidomide and prescription and approval and code warning and fetus).clm.	US-PGPUB; USPAT; UPAD	OR	ON	2011/03/02 20:17
L1	20	(thalidomide and prescription and approval and code warning and fetus).clm.	USPAT; UPAD	OR	ON	2011/03/02 20:17
L3	18	(thalidomide and prescription and approval and code warning and fetus and contraception).clm.	US-PGPUB; USPAT; UPAD	OR	ON	2011/03/02 20:18
L12	18	(thalidomide and prescription and approval and code warning and fetus and contraception and pharmacy).clm.	US-PGPUB; USPAT; UPAD	OR	ON	2011/03/02 20:53

3/2/2011 9:42:22 PM
C:\Documents and Settings\krajan\My Documents\EAST\Workspaces\11437551.wsp

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
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Alexandria, Virginia 22313-1450
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

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23377 7590 04/26/2011
WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/437,551	05/19/2006	Bruce A. Williams	CELG-0508	3533

TITLE OF INVENTION: METHODS FOR DELIVERING A DRUG TO A PATIENT WHILE RESTRICTING ACCESS TO THE DRUG BY PATIENTS FOR WHOM THE DRUG MAY BE CONTRAINDICATED

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EXAMINER	ART UNIT	CLASS-SUBCLASS
RAJAN, KAI	3769	600-300000

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2. For printing on the patent front page, list
(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 Woodcock Washburn, LLP
2
3

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE: Celgene Corporation
(B) RESIDENCE: (CITY and STATE OR COUNTRY): Warren, New Jersey

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:
☒ Issue Fee
☒ Publication Fee (No small entity discount permitted)
☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
☐ A check is enclosed.
☐ Payment by credit card. Form PTO-2038 is attached.
☒ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number 23-3050 (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.
☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature /Stephanie A. Barbosa/ Date May 3, 2011
Typed or printed name Stephanie A. Barbosa Registration No. 51,430

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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PTO/SB/47 (03-09)
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Fax to:
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INSTRUCTIONS: The issue fee must have been paid for application(s) listed on this form. In addition, only an address represented by a Customer Number can be established as the fee address for maintenance fee purposes (hereafter, fee address). A fee address should be established when correspondence related to maintenance fees should be mailed to a different address than the correspondence address for the application. **When to check the first box below**: If you have a Customer Number to represent the fee address. **When to check the second box below**: If you have no Customer Number representing the desired fee address, in which case a completed Request for Customer Number (PTO/SB/125) must be attached to this form. For more information on Customer Numbers, see the Manual of Patent Examining Procedure (MPEP) § 403.

For the following listed application(s), please recognize as the "Fee Address" under the provisions of 37 CFR 1.363 the address associated with:

☑ Customer Number: 000075490

OR

☐ The attached Request for Customer Number (PTO/SB/125) form.

PATENT NUMBER (if known)	APPLICATION NUMBER
	11/437,551

Completed by (check one):

☐ Applicant/Inventor

/Stephanie A. Barbosa/
Signature

☑ Attorney or Agent of record 51,430 (Reg. No.)

Stephanie A. Barbosa
Typed or printed name

☐ Assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)

215-568-3100
Requester's telephone number

☐ Assignee recorded at Reel _____ Frame_____

May 3, 2011
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more that one signature is required, see below*.

☑ *** Total of 1 forms are submitted.**

This collection of information is required by 37 CFR 1.363. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1. 11 and 1.14. This collection is estimated to take 5 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313- 1450. DO NOT SEND COMPLETED FORMS TO THIS ADDRESS.
SEND TO: Mail Stop M Correspondence, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.
If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Patent Application Fee Transmittal

Application Number:	11437551
Filing Date:	19-May-2006
Title of Invention:	METHODS FOR DELIVERING A DRUG TO A PATIENT WHILE RESTRICTING ACCESS TO THE DRUG BY PATIENTS FOR WHOM THE DRUG MAY BE CONTRAINDICATED
First Named Inventor/Applicant Name:	Bruce A. Williams
Filer:	Stephanie A. Barbosa
Attorney Docket Number:	CELG-0508

Filed as Large Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Utility Appl issue fee	1501	1	1510	1510
Publ. Fee- early, voluntary, or normal	1504	1	300	300

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
		Total in USD ($)		**1810**

Electronic Acknowledgement Receipt

EFS ID:	10010430
Application Number:	11437551
International Application Number:	
Confirmation Number:	3533
Title of Invention:	METHODS FOR DELIVERING A DRUG TO A PATIENT WHILE RESTRICTING ACCESS TO THE DRUG BY PATIENTS FOR WHOM THE DRUG MAY BE CONTRAINDICATED
First Named Inventor/Applicant Name:	Bruce A. Williams
Customer Number:	23377
Filer:	Stephanie A. Barbosa
Filer Authorized By:	
Attorney Docket Number:	CELG-0508
Receipt Date:	03-MAY-2011
Filing Date:	19-MAY-2006
Time Stamp:	15:35:08
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$1810
RAM confirmation Number	2001
Deposit Account	233050
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Issue Fee Payment (PTO-85B)	CELG-0508-IssueFee.pdf	106856 7a10ef9ae2354fc622a8c1609e7dcb54afb552d4	no	1
Warnings:					
Information:					
2	Change of Address	CELG-0508-FeeAddress.pdf	318377 0d2d3f03e96a5b7f6ad3d6c84f5da4ab73498f14	no	2
Warnings:					
Information:					
3	Fee Worksheet (PTO-875)	fee-info.pdf	32294 bc43ec1b59e731f95e04a0414deb81581ad545a7	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	457527		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Form PTO-1449 Modified

List of Patent and Publications
Cited by Applicant
(Use several sheets if necessary)

U.S. Department of Commerce
Patent and Trademark Office

Docket No. CELG-0508	Application No. 11/437,551
Applicant Bruce A. Williams, et al.	
Filing Date May 19, 2006	Group 3736
Confirmation No. 3533	

U. S. PATENT DOCUMENTS

Examiner Initial		Document No.	Date	Name	Class	Subclass
	1	5,299,121	03/20/94	Brill, et al.	600	301
	2	5,594,637	01/14/97	Eisenberg, et al.	600	300
	3	5,619,991	04/15/97	Sloane	600	300
	4	5,660,176	08/26/97	Iliff	600	300
	5	5,832,449	11/03/98	Cunningham	705	3
	6	5,845,255	12/01/98	Mayaud	705	3
	7	5,974,203	10/26/99	Tadokoro, et al.	382	309
	8	6,014,631	01/11/00	Teagarden, et al.	705	3
	9	6,045,501	04/04/00	Elsayed, et al.	600	300
	10	6,055,507	04/25/00	Cunningham	705	3
	11	6,063,026	05/16/00	Schauss, et al.	600	300
	12	6,128,620	10/03/00	Pissanos, et al.	707	102
Change(s) applied	13	6,131,090	10/10/00	Basso, Jr., et al.	706	23
to document, /S.R.K./ 5/5/2011	14	6,202,923 B1	03/20/01	Boyer, et al.	235	375
	15	6,315,720 B1	11/13/01	Williams, et al.	600	300
	16	6,561,976 B2	05/13/03	Elsayed, et al.	600	300
	17	6,561,977 B2	05/13/03	Williams, et al.	600	300
6,561,976	18	~~6,561,978~~ B2	05/13/03	Elsayed, et al.	128	920
	19	6,755,784	06/29/04	Williams, et al.	600	300
	20	6,755,784	06/2004	Williams et al.	600	300

EXAMINER	/Michael Astorino/	DATE CONSIDERED	04/27/2008

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /MA/

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/437,551	06/14/2011	7959566	CELG-0508	3533

23377 7590 05/25/2011

WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment is 139 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Data Management (ODM) at (571)-272-4200.

APPLICANT(s) (Please see PAIR WEB site http://pair.uspto.gov for additional applicants):

Bruce A. Williams, Flemington, NJ;
Joseph K. Kaminski, Hampton, NJ;

AO 120 (Rev. 08/10)

TO:	**Mail Stop 8 Director of the U.S. Patent and Trademark Office P.O. Box 1450 Alexandria, VA 22313–1450**	**REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK**

In Compliance with 35 U.S.C. § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the **U.S. District Court for the District of New Jersey** on the following:
___ Trademarks or **X** Patents. (____ the patent action involves 35 U.S.C. § 292.)

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT
2:15–cv–00697–SDW–SCM	1/30/2015	NEWARK, NJ
PLAINTIFF CELGENE CORPORATION		DEFENDANT LANNETT HOLDINGS, INC.

PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1 ~~See Attached Complaint~~		
2 6045501		
3 6315720		
4 6561976		
5 6561977		

In the above––entitled case, the following patent(s)/ trademark(s) have been included:

DATE INCLUDED	INCLUDED BY ___ Amendment ___ Answer ___ Cross Bill ___ Other Pleading

PATENT OR TRADEMARK NO.	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
1 6735784		
2 6869399		
3 7141018		
4 7959564		
5 8204763		

In the above––entitled case, the following decision has been rendered or judgement issued:

DECISION/JUDGEMENT

CLERK	(BY) DEPUTY CLERK	DATE
William T. Walsh	s/ Christine Melillo	1/30/2015

Copy 1—Upon initiation of action, mail this copy to Director Copy 3—Upon termination of action, mail this copy to Director
Copy 2––Upon filing document adding patent(s), mail this copy to Director Copy 4—Case file copy